KONGRES FARMACEUTA
U BOSNI I HERCEGOVINI
SA MEĐUNARODNIM UČEŠĆEM

SARAJEVO, 10.10-13.10.2019.

NOVI TRENDOVI U FARMACIJI

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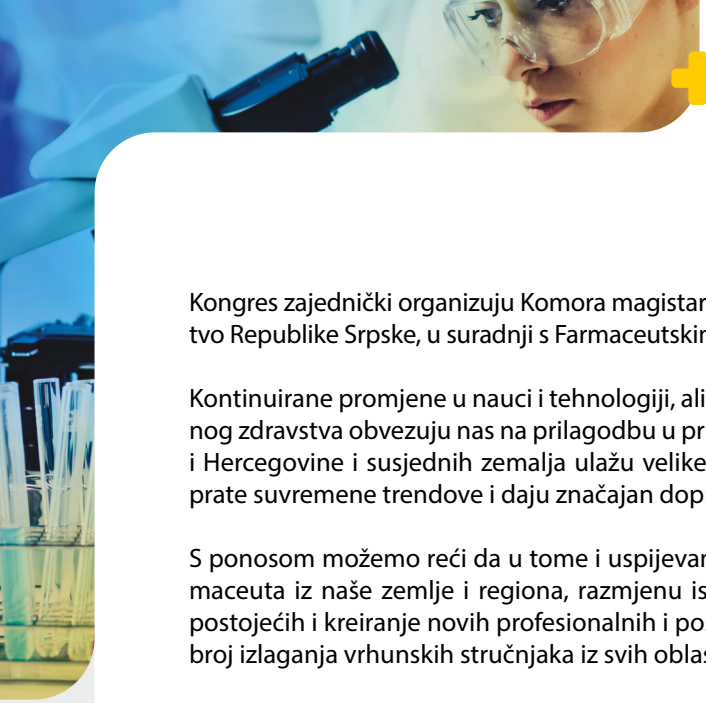

NOVI TRENDOVI U FARMACIJI

Kongres zajednički organizuju Komora magistara farmacije Federacije Bosne i Hercegovine i Farmaceutsko društvo Republike Srpske, u suradnji s Farmaceutskim fakultetima Univerziteta u Sarajevu, Tuzli, Banja Luci i Mostaru.

Kontinuirane promjene u nauci i tehnologiji, ali i društvenim prilikama koje donose nove izazove i na polju javnog zdravstva obvezuju nas na prilagodbu u pristupu obrazovanju, nauci i praksi u farmaciji. Farmaceuti Bosne i Hercegovine i susjednih zemalja ulažu velike napore da u sopstvenom i razvoju svoje struke u potpunosti prate suvremene trendove i daju značajan doprinos očuvanju i unapređenju zdravlja.

S ponosom možemo reći da u tome i uspijevamo. Ovaj kongres bit će prilika za prezentiranje postignuća farmaceuta iz naše zemlje i regiona, razmjenu iskustva s kolegama iz drugih dijelova Evrope i svijeta, jačanje postojećih i kreiranje novih profesionalnih i poslovnih veza. U okviru osam sekcija kongresa očekuje vas veliki broj izlaganja vrhunskih stručnjaka iz svih oblasti farmacije.

Srdačno pozivamo kolege farmaceute i druge stručnjake s profesionalnim interesima vezanim za farmaciju da svojim učešćem doprinesu uspjehu kongresa, s kojeg ćete zasigurno ponijeti neka nova znanja i lijepe uspomene.

Želimo Vam toplu dobrodošlicu u Sarajevo, jedinstveni spoj Istoka i Zapada!

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The Congress is co-organised by the Chamber of Pharmacists of the Federation of Bosnia and Herzegovina and the Pharmaceutical Society of Republika Srpska, in cooperation with faculties of pharmacy of the University in Sarajevo, Tuzla, Banja Luka, and Mostar.

Continuous changes in science, technology, and society that bring about new challenges in the area of public health require us to adjust our approach to education, science, and practice in pharmacy.

Pharmacists of Bosnia and Herzegovina and the neighbouring countries make great efforts to follow the modern trends in their personal development and in the development of their profession and to provide significant contributions to health preservation and improvement. We are proud to be able to say that we are succeeding in this. This Congress is going to be an opportunity to present accomplishments of pharmacists from our country and the region, to exchange experiences with our colleagues from other parts of Europe and the world, as well as to strengthen the existing and create new professional and business ties. Within eight sections of the Congress, you will have an opportunity to attend presentations of top experts from all fields of pharmacy.

We warmly welcome you to Sarajevo – where East and West meet!

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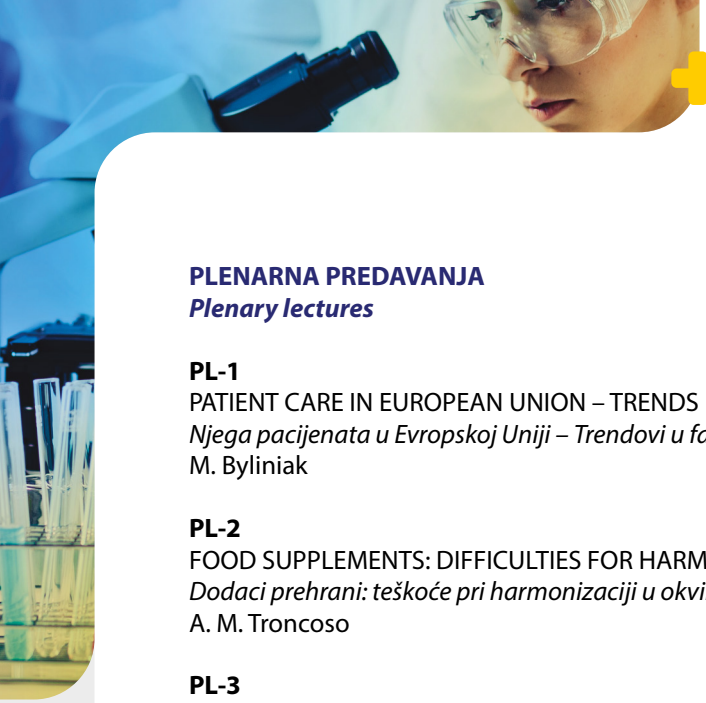

NOVI TRENDOVI
U FARMACIJI

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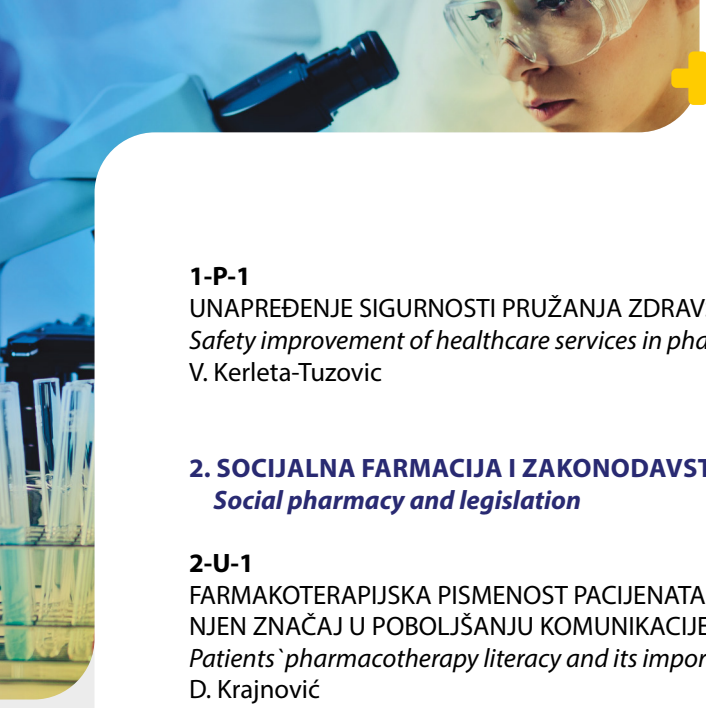

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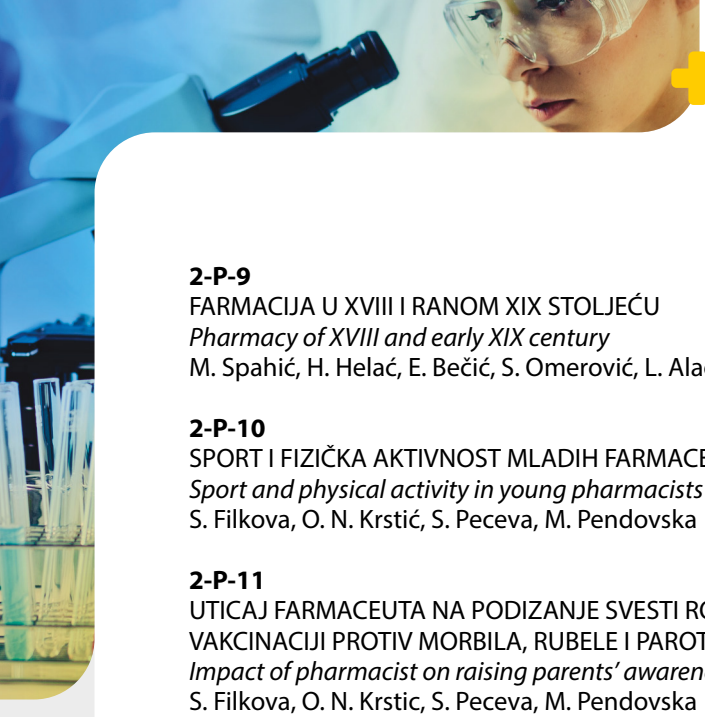

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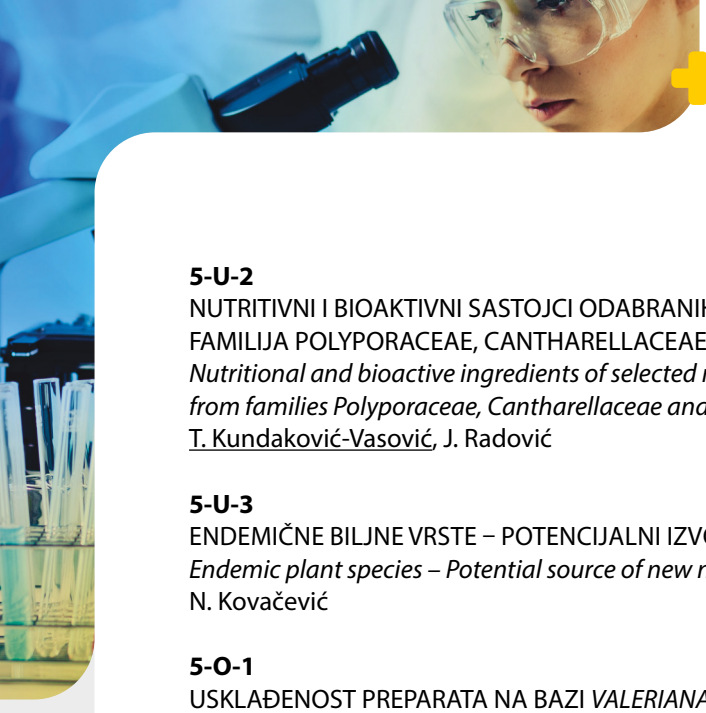

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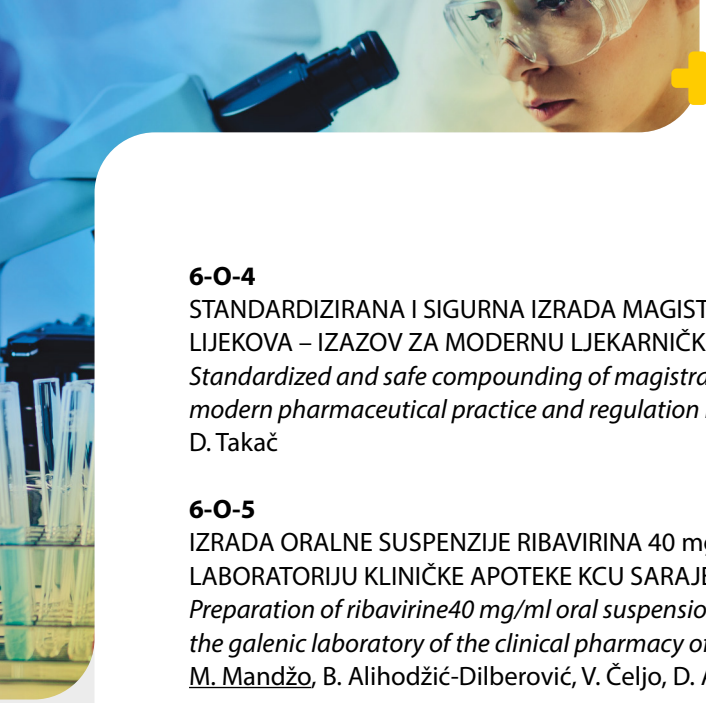

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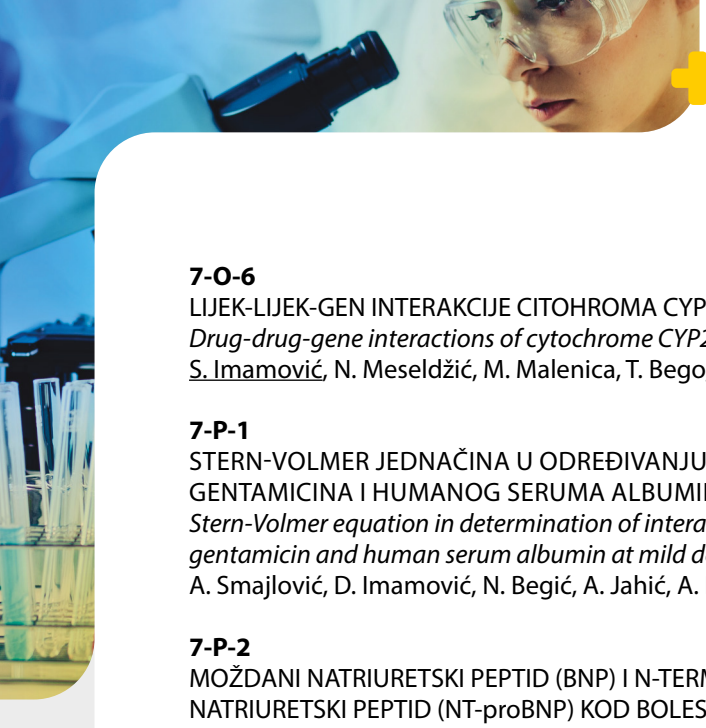

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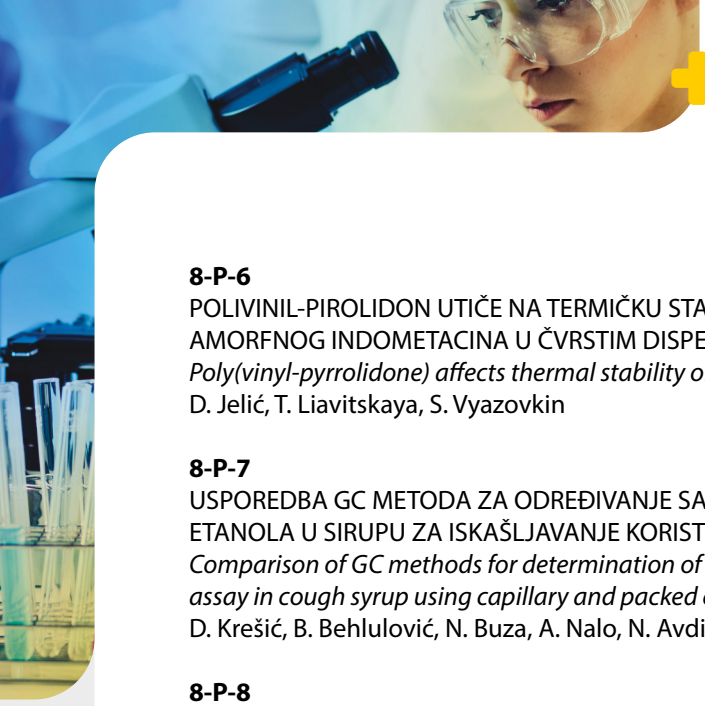

SADRŽAJ
CONTENT

PLENARNA PREDAVANJA

PLENARY LECTURES

NJEGA PACIJENATA U EVROPSKOJ UNIJI – TRENDOVI U FARMACEUTSKIM USLUGAMA

M. Byliniak

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Demografska slika Evrope mijenja se iz godine u godinu. Broj starijih osoba raste, a istovremeno u mnogim zemljama broj ljekara i medicinskih sestara se smanjuje. To rezultira smanjenjem pristupa medicinskim uslugama za pacijente, ograničavanjem poštivanja i pridržavanja, te povećanjem troškova farmakoterapije. Odgovor na ovaj trend je promjena u percepciji uloge apoteka i farmaceuta tako što ih se strogo uključuje u zdravstveni sistem omogućavanjem pružanja specijaliziranih farmaceutskih usluga u apotekama. Ovo predavanje ima za cilj predstaviti širu sliku perspektivnih trendova u primjeni apotekarskih usluga i raspravljati o najvažnijim događajima posljednjih mjeseci u području farmaceutske njege.

LITERATURA

[1] Sluge i aktivnosti evropskih apoteka, Baza podataka PGEU-a

KLJUČNE RIJEČI: farmacija, farmaceutska njega, usluge za pacijente

PATIENT CARE IN EUROPEAN UNION – TRENDS IN PHARMACEUTICAL SERVICES

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The demographic image of Europe is changing from year to year. The number of elderly people is increasing, in many countries the number of doctors and nurses is declining. This results in a decrease in patients' access to medical services, limiting compliance and adherence and an increase in pharmacotherapy costs. The answer to this trend is a change in the perception of the role of pharmacies and pharmacists by strictly including them in the health care system by enabling the provision of specialized pharmaceutical services in pharmacies. This speech aims at presenting big picture of perspective trends in the implementation of pharmacy services and discussing the most hot events of recent months in the field of pharmaceutical care.

REFERENCES

[1] European Community Pharmacy Services & Activities, PGEU Database

KEY WORDS: pharmacy, pharmaceutical care, patient, services

DODACI PREHRANI: TEŠKOĆE PRI HARMONIZACIJI U OKVIRU EU

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UVOD I CILJ

Potrošnja dodataka prehrani u EU znatno se povećala posljednjih godina. Postojeći pravni okvir predstavlja Direktiva iz 2002. (Direktiva 2002/46/EZ) koja ih definira kao prehrambene proizvode čija je svrha nadopunjavanje uobičajene prehrane i sastoje se od koncentriranih izvora hranjivih tvari ili drugih tvari koje imaju prehrambeni ili fiziološki učinak, u jednostavnom ili kombiniranom obliku, koje se stavljaju u promet u obliku doza, tj. kapsula, tableta, pilula i drugih sličnih oblika, a koje se moraju uzimati u malim jediničnim količinama. Biljni lijekovi zasebna su kategorija regulirana Direktivom 2004/27/EZ. S pravnog stajališta u EU-u smatraju se hranom za sve namjene i stoga su regulirani Uredbom 178/2002 jer ne postoji posebna kategorija dodataka prehrani, te samim tim nisu podvrgnuti nikakvoj prethodnoj procjeni sigurnosti prije stavljanja na tržište. Iako je iz perspektive pitanja koje se tvari smatraju dodacima prehrani slučaj dodataka prehrani (vitamina i minerala) jasan, to nije slučaj s „drugim supstancama", za koje postoji značajan pravni jaz. Evropska komisija vodi popis tvari za koje se sumnja da imaju štetne učinke na zdravlje i za koje se sumnja da imaju štetne učinke.

METODE

Provodi se pregled trenutnih procjena rizika i praksi upravljanja rizikom u različitim zemljama EU.

REZULTATI

Kao rezultat gore navedenog, pravni okvir za dodatke prehrani u Evropi nije u potpunosti usklađen i ista supstanca ili proizvod koji se smatra dodatkom prehrani u jednoj evropskoj državi možda ne mora imati taj status u drugoj zemlji EU, što rezultira neravnotežom na unutarnjem tržištu. Posljednjih godina EFSA je uložila značajne napore za procjenu maksimalnih dopuštenih unosa vitamina i minerala (podnošljivi gornji nivo unosa), ali nije došlo do njenog prenošenja u zakonodavstvo. Može se reći da postoji nekoliko neriješenih problema koji utiču na ove proizvode: učinkovitost, sigurnost, nedostatak pravne usklađenosti. te aspekti povezani s čistoćom i stabilnošću. Tako proizvođači na etiketi izjavljuju da određeni proizvod sadrži određenu količinu ekstrakta botaničke vrste, ali ništa nije naznačeno u odnosu na sadržaj bioaktivnih spojeva, što može rezultirati neučinkovitošću ili predoziranjem. Stoga nije iznenađujuće da je posljednjih godina broj obavještenja o dodacima prehrani eksponencijalno porastao u evropskom sistemu upozorenja o hrani (RASFF). Također treba napomenuti da se u primjeni Uredbe 1924/2006 o prehrambenim i zdravstvenim tvrdnjama koje se navode na pakovanju hrane, predloženi zahtjev mora prvo procijeniti i odobriti kako bi se postavila bilo kakva tvrdnja o njegovom uticaju na zdravlje.

ZAKLJUČCI

Potrebni su dodatni napori za usklađivanje pravila koja reguliraju tržište dodataka prehrani u EU.

LITERATURA

[1] Direktiva 2002/46/EC Evropskog palamenta i Vijeća od 10. juna 2002. o usklađivanju zakona država članica u odnosu na dodatke prehrani

[2] Evropska agencija za sigurnost hrane (EFSA) https://www.efsa.europa.eu/en/topics/topic/food-supplements

KLJUČNE RIJEČI: dodaci prehranim, usklađivanje, upravljanje rizicima, procjena rizika, sigurnost

FOOD SUPPLEMENTS: DIFFICULTIES FOR HARMONIZATION IN THE EU FRAME

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INTRODUCTION AND OBJECTIVE

The consumption of food supplements in the EU has increased substantially in recent years The existing legal framework is a Directive dating 2002 (Directive 2002/46 /EC) that defines them as food products whose purpose is to complement the normal diet and consist of concentrated sources of nutrients or other substances that have a nutritional or physiological effect, in simple or combined form, marketed in dosed form, ie capsules, pills, tablets, and other similar forms, and which must be taken in small unit quantities. Herbal medicinal products are a separate category regulated by Directive 2004/27/EC. From the legal point of view in the EU they are considered food for all purposes and therefore are regulated by Regulation 178/2002, since there is no special category for food supplements, and therefore they are not subjected to any prior assessment about its safety, before placing on the market. Although from the point of view of what substances are considered food supplements, the case of nutrients (vitamins and minerals) is clear, it is not so for the case of these "other substances", for which there is a considerable legal gap . While the European Commission maintains a list of substances known or suspected to have adverse effects on health and whose use is controlled.

METHODS

A review of the current risk assesment and risk management practices in the different EU countries is performed.

RESULTS

As a result of the above, the legal framework for food supplements in Europe is not fully harmonized and the same substance or product that is considered a food supplement in one European country may not have such consideration in another EU country, resulting in internal market imbalances.

In recent years, EFSA has made a considerable effort to assess the maximum levels of allowable intake (tolerable upper intake level) for vitamins and minerals, but its transfer to the legislation has not taken place. It can be said that there are several unresolved problems that affect these products: efficiency, safety, lack of legal harmonization. Aspects related to purity and stability. Thus, the producers declare on the label that a certain product contains a certain amount of an extract of a botanical species, but nothing is indicated regarding the content of bioactive compounds, which may result in inefficiency or overdose. It is not surprising, therefore, that in recent years the number of notifications in the European food alert system (RASFF) for food supplements has grown exponentially.

It should also be noted, in relation to its effectiveness, that in application of Regulation 1924/2006 on nutritional and health claims of food, in order to make any claim regarding its effect on health, the proposed claim must be previously evaluated and authorized.

CONCLUSIONS

An additional effort is needed for the aim of harmonizing the rules governing food supplements market in the EU

REFERENCES

[1] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements

[2] European Food Safety Authority (EFSA) https://www.efsa.europa.eu/en/topics/topic/food-supplements

KEY WORDS: food supplements, harmonization, risk management, risk assesment, safety

TRENUTNI TRENDOVI I IZAZOVI U OBLASTI ISTRAŽIVANJA BILJNIH LIJEKOVA

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U Evropskoj uniji Komisija za biljne lijekove (HMPC) pri Evropskoj agenciji za lijekove (EMA) ocjenjuje javno dostupnu naučnu literaturu o učinkovitosti i sigurnosti biljnih pripravaka. Za razliku od priznate vrijednosti biljnih lijekova u široj javnosti, procjena objavljenih podataka otkriva vrlo često velike razlike. U skladu s tim, dovoljno dokaza o učinkovitosti i sigurnosti moglo bi se navesti samo za pripravke iz 25 biljnih lijekova od više od 200 procijenjenih lijekova. Samo za 12 tradicionalno korištenih biljnih pripravaka pronađen je dovoljno dokumentiran nivo sigurnosti koji podržava objavu takozvanog „unosa na popis" koji olakšava znatno pojednostavljeni postupak registracije biljnih lijekova.

Dokaz kvaliteta biljnih lijekova prema standardima definiranim u Evropskoj farmakopeji trebao bi garantirati optimalan materijal za biljne lijekove. Međutim, za mnoge biljne lijekove nije poznat uticaj uvjeta uzgoja, razvoja biljaka prije žetve i uvjeta nakon berbe.

Buduća istraživanja farmakognozije trebala bi pokušati popuniti praznine. Izazovni primjeri mogu biti:

- Istraživanje kvaliteta: inovativni pristupi kontroli kvaliteta (npr. dokumentacija nabavnog lanca, istraživanje promjena u obliku sastojaka zbog starosti biljke, vremena berbe, uvjeta sušenja, uvjeta skladištenja; koncepti za definiranje opće kvalitete umjesto testiranje pojedinačne tvari); dublji uvid u sastav biljnih pripravaka kako bi se bolje definirali pripravci i postigla visoka razina konzistencije od pripreme do pripreme;
- Neklinička istraživanja: usredotočiti se na farmakološke modele koji se mogu povezati s kliničkim učinkom (npr. korištenje koncentracija koje se mogu postići kod ljudi); procjena stvarnog uticaja neklinič-kih podataka o toksičnosti na kliničku sigurnost; bolje razumijevanje farmakokinetike sastojaka za koje se smatra da su relevantni za aktivnost;
- Klinička istraživanja: klinička farmakokinetička ispitivanja; studije interakcije; dokumentacija o upotrebi u medicinskoj praksi (općenito, kod djece,…).

Istraživanje bi trebalo uzeti u obzir trenutne smjernice za lijekove iz odgovarajućeg područja.

Odricanje od odgovornosti:
Izneseni stavovi ne predstavljaju nužno stajalište austrijske Agencije za lijekove i medicinska sredstva (AGES Medizinmarktaufsicht / BASG) niti (komisije) Europske agencije za lijekove.

KLJUČNE RIJEČI: biljni medicinski proizvodi, kvalitet, sigurnost, učinkovitost, toksičnost

CURRENT TRENDS AND CHALLENGES FOR RESEARCH ON HERBAL MEDICINES

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In the European Union, the Committee on Herbal Medicinal Products (HMPC) at the European Medicines Agency (EMA) assesses publicly available scientific literature concerning efficacy and safety of herbal preparations. In contrast to the esteemed value of herbal medicines in the general public the assessment of published data revealed very often big gaps. Consequently, only for preparations from 25 herbal drugs out of more than 200 assessed ones a sufficient evidence for efficacy and safety could be assigned. Only for 12 traditionally used herbal preparations a sufficiently documented level of safety could be found to support a publication of a so called 'list entry' which facilitates a considerably simplified registration procedure of herbal medicinal products.

The proof of quality of herbal drugs according to the standards as defined in the European Pharmacopoeia should guarantee optimal material for herbal medicines. However, for many herbal drugs the impact of conditions of cultivation, plant development before harvest and post-harvest conditions on the constituents is not known.

Future research in pharmacognosy should try to fill the gaps. Challenging examples could be:

- Quality research: innovative approaches for quality control (e.g. documentation of the supply chain, investigation on changes in the pattern of constituents due to age of plant, harvest time, drying conditions, storage conditions; concepts to define an overall quality instead of single substance assays); deeper insight in the composition of herbal preparations in order to better define the preparations and achieve a high level of batch-to-batch consistency;
- Non-clinical research: focus on pharmacological models which can be related to a clinical effect (e.g. using concentrations which can be achieved in humans); evaluation of the actual impact of non-clinical toxicity data on clinical safety; better understanding of the pharmacokinetics of constituents which are considered to be relevant for the activity;
- Clinical research: clinical pharmacokinetic studies; interaction studies; documentation of the use in the medical practice (in general, in children, …).

Research should consider current guidelines for medicinal products in the respective field.

Disclaimer:
The views presented do not necessarily represent the views of the Austrian Medicines and Medical Devices Agency (AGES Medizinmarktaufsicht / BASG) nor of the (committees of the) European Medicines Agency.

KEY WORDS: herbal medicinal products, quality, safety, efficacy, toxicity

APOTEKARSKA I BOLNIČKA FARMACIJA

COMMUNITY AND HOSPITAL PHARMACY

UVODNO PREDAVANJE

ULOGA BIZNISA U FARMACEUTSKOJ PRAKSI

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Apoteke svoju djelatnost obavljaju u ekonomski konkurentnoj sredini i moraju znati osnovna pravila i izvore financiranja. Kako bi obezbedile opstanak i financijsku održljivost djelatnosti, neophodno je steći osnovna znanja iz menadžmenta financijskih resursa u ustanovi. U ovom izlaganju ćemo prodiskutovatai o važnosti poznavanja osnove menadžiranja kao jedan od najvažnijih elemenata za dobro poslovanje apoteka u finansijskom smislu.

Farmaceuti radije ramišljaju sa aspekta zdravstvene zaštite i terapije nego sa aspekta finansija i prodaje. Ipak, moramo prihvatiti činjenicu da su apoteke takođe i trgovine u maloprodaji i razmišljati o održivosti biznisa i njegovom unapređivanju. Tržište lijekova i medicinskih sredstava ne podliježe čisto ekonomskim zakonitostima, već je regulisano i kontrolisano od strane države posebnom regulativom: cijene lijekova, apotekarskih usluga i uslovi poslovanja. Takođe, farmaceuti moraju poštovati i svoje etičke kodekse. To ograničava mogućnosti poslovanja u ekonomskom smislu.

Cijene lijekova su regulirane i ograničene referiranjem, generičke politike i racionalizacija propisivanja smanjuje obim rada apoteka, fondovi ograničavaju obim i cijenu farmaceutske usluge, farmaceutske politike stimulišu smanjenje potrošnje lijekova i pad njihovih cijena. Za uspješno poslovanje apoteka, menadžeri moraju biti preduzimljivi, u stalnoj potrazi za rastom i širenjem poslovanja. Moraju prepoznati trendove i naučiti kada i kako treba napraviti promjene u svom poslovanju i strategiji. Moderni i uspješni farmaceut mora pratiti financijsko stanje apoteke, mogućnosti investiranja i razvoja, izražene potrebe pacijenata u svojoj okolini, potrebe i interese društva u oblasti javnog zdravlja, razvoj novih tehnologija, mora razvijati vlastite vještine komuniciranja i finansijskog poslovanja i mora naći načana da promoviše svoj rad i rad apoteke i naplatiti svoje usluge.

Apoteke su nerazdvojni deo zdravstvenog sistema i njihov financijski opstanak i razvoj je važan za društvo i državu, zato moramo stalno promovisati i predstavljati svoj rad i benefite koje društvo dobija zahvaljujući dobrom poslovanju apoteka.

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KLJUČNE RIJEČI: apoteka, farmaceut, menadžment, finansisko poslovanje

ROLE OF BUSINESS IN PHARMACEUTICAL PRACTICE

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According to the fact that pharmacies realize their activities in economically competitive environment, essential part for optimal function is to get knowledge about basic rules and sources of funding.

In order to ensure the survival and sustainability of financial activities, it is necessary to acquire basic knowledge about the management of financial resources of the institution. So, in this presentation we will discuss about the importance of pharmacist knowledge about basis of management as crucial part for profitable pharmacy business from financial aspect. Despite the fact that the principal task of the pharmacist is to identify, resolve and prevent drug-related problems, in order to maximize profit potential pharmacists must gain knowledge about financial management. Therefore, pharmacy as retail store, need to focus on hiring good staff, maximizing front-end space for high-profit sales and attracting and retaining more patients.

Market of medicines and medical devices is not regulated only by economic laws, but is based also on state regulatory policies for: prices and the pharmaceutical market, pharmacy services and also business conditions. Also, pharmacists must respect the code of ethics for pharmaceutical practice, which strongly limits business opportunities from economic aspect. Drug prices are regulated and limited by reference pricing. Generic prescribing policies and streamlining reduces the workload of pharmacies, funds limit the scope and cost of pharmaceutical services and pharmaceutical policy stimulate the reduction of drug consumption and prices. A modern and successful pharmacist must monitor the financial condition of the pharmacy, the possibilities of investment and development and also of the expressed needs of the patients. Generally, pharmacist should possess a combination of comprehensive therapeutic knowledge, experience, problem-solving skills, and judgment.

As conclusion we can say that pharmacies are inseparable part of healthcare system and their financial development is important for society and the state, so we must constantly promote and present our work and benefits that society receives thanks to the good pharmacy business and practice.

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KEY WORDS: pharmacist, knowledge, business, financial support

UVODNO PREDAVANJE

PARADIGMA PRIMENE BISFOSFONATA U PRIMARNOJ ZDRAVSTVENOJ ZAŠTITI - NEŽELJENI EFEKTI, KAKO IH SPREČITI

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UVOD I CILJ
Terapija bifosfonatima se moze koristiti kod osteporoze, Padžetove bolesti, odredjenih formi karcinoma dojke i multiplog mijeloma. Sa druge strane lekovi iz ove grupe imaju dosta neželjenih efekata koji predstavljaju značajan medicinski i ekonomski problem.

METODE
Istraživanje je sprovedeno kao sistematska pretraga dostupne literature nakon čega je vršena selekcija visoko kvalitetnih dokaza o terapiji bifosfonatima. Bezbednost bifosfonata je sumirana kroz podatke iz prikaza slučajeva, preglednih radova i kliničkih studija. Pretraga literature je vršena prema sledećim terminima ((("adverse effects"[Subheading] OR ("adverse"[All Fields] AND "effects"[All Fields]) OR "adverse effects"[All Fields]) AND (("prevent"[All Fields]) AND ("adverse effects"[Subheading] OR ("adverse"[All Fields] AND "effects"[All Fields]) OR "bisphosphonate"[All Fields]))) AND ("primary health care"[MeSH Terms].

REZULTATI
Početna pretraga je rezultovala ishodom od 30 članaka od koji su 8 bili u vezi neželjenih efekata bifosfonata u primarnoj zdravstvenoj zaštiti. Dužina primene bifosfonata je esencijalna komponetna u vezi sa povećanjem rizika od neželjenih efekata. Dodatni faktori su bili vrsta bifosfonata, način primene, prisustvo komorbiditeta i interakcije sa lekovima. Medicinske baze poput MEDLINE, EBSCO i Scopus/Elsevier pokazuju konzistentne podatke u pogledu najčešćih neželjenih efekata kao što su ezofagealna erozija, hipokalcemija, atipične frakture, atrijalna fibrilacija, bolovi u mišićno koštanom sistemu, okularna inflamacija, smanjenje bubrežne funkcije i osteonekroza vilice. Interesantni podaci su prikazi osteonekroze slušnog kanala kao i klinička studija o karpalnom tunel sindromu used primene bifosfonata. Zolendronska kiselina je bifosfonat sa najvećom stopom prijavljenih neželjenih događaja. Na osnovu pubikovanih podataka raloksifen ne dovodi do smanjena sigurnih ishoda dok teraparatid i denosuman mogu imati određeni uticaj na bezbedonosni profil.

ZAKLJUČCI
Pristup u prevenciji neželjenih efekata bifosfonata podrazumeva razmatranje svih potencijalnih faktora koji mogu da utiču na bezbedonosni profil pre započinjanja terapije.

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KLJUČNE RIJEČI: bisfosfonati, štetne posljedice, sigurnost, pregled literature

PARADIGM OF THE USE OF BISPHOSPHONATES IN PRIMARY HEALTH CARE - SIDE EFFECTS, HOW TO PREVENT THEM

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INTRODUCTION AND OBJECTIVE
Bisphosphonates therapy can be use at osteoporosis, Paget disease, some case of breast cancer and multiple myeloma.On the other hand, these drugs have a wide range of serious side effects which represent great medical and economy problem.

METHODS
Our research was based on systematic search of avaiable literature and selection of high-quality evidence of bisphosphonates therapy. Safety of bisphosphonates therapy were summarized according to available data from case report, review and clinical trial. Research was conducted as the following(((“adverse effects”[Subheading] OR (“adverse”[All Fields] AND “effects”[All Fields]) OR “adverse effects”[All Fields]) AND ((“prevent”[All Fields]) AND (“adverse effects”[Subheading] OR (“adverse”[All Fields] AND “effects”[All Fields]) OR “bisphosphonate”[All Fields]))) AND (“primary health care”[MeSH Terms].

RESULTS
An initial review resulted with 30 articles from which 8 articles were addrese to the adverse effects at primary health care. Duration of biphosponate consumation is one of a key element that may lead to higher risk of adverse effects. Additional factors were type of bisphosponate, type of administration, presence of comorbidity and drug interactions. Medical databases such as MEDLINE, EBSCO and Scopus/Elsevier showed a consistent data in regards of the most offten adverse events such as oesophageal destruction, decrease level of calcium, atypical fractures, atrial fibrillation, musculoskeletal pains, ocular inflammation, impairment of renal function and osteonecrosis of the jaw. Interesting data is report of osteonecrosis of the ear canal and clinical study of carpal tunel syndrome. Zolendronic acid was the bisphosphonate with the highest rate of the adverse reports. According to published data raloxifene does not decrase safety outcomes while teriparatide and denosumab can have some influence on safety outcomes.

CONCLUSIONS
Approaches in the prevention of adverse effects of bisphosphonate should be consideration of all mentioned factors before starting therapy.

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KEY WORDS: bisphosphonate, adverse event, safety, literature research

UVODNO PREDAVANJE

BISFOSFONATIMA IZAZVANA NEKROZA VILICE – OPASNA REALNOST

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UVOD

Bisfosfonatima izazvana nekroza kosti vilice (BRONJ) predstavlja primarno neželjeni efekat primene bisfosfonata, naročito kada se primenjuje u visokim dozama kod pacijenata sa karcinomom i koštanim metastazama. Mnoge stomatološke procedure, poput ekstrakcije zuba, oralne i parodontalne hirurgije i resektivne koštane hirurgije vilica mogu isprovocirati nastanak BRONJ. Interesantno je primetiti da se BRONJ može razviti i primarno, čak i bez hirurške intervencije.

MATERIJAL I METODE

Sistematska elektronska pretraga dostupne literature i izbor visoko-kvalitetnih dokaza o BRONJ urađena je korišćenjem MEDLINE, EBSCO i SCOPUS baza korišćenjem odgovarajućih ključnih reči i termina. Uključili smo podatke iz kliničkih studija, revijskih radova i prikaza slučajeva. Istraživanje je izvedeno prema sledećim terminima ((„bisphosphonate osteonecrosis of the jaw"[Subheading] OR („bisphosphonates „[All Fields] AND „osteonecrosis"[All Fields]) OR „bisphosphonate osteonecrosis"[All Fields]) AND ((„prevent"[All Fields]) AND („adverse effects"[Subheading] OR („bisphosphonates"[All Fields] AND „jaw bone"[All Fields]) OR „bisphosphonates"[All Fields]))) AND („medical related osteonecrosis of the jaw"[MeSH Terms])).

REZULTATI

Inicijalna pretraga najpre je obuhvatila 2149 naučnih članaka. Primenili smo dodatne filtere pretrage (uključili smo humane studije, članke publikovane u poslednje 3 godine, radove sa dostupnim punim tekstom) i konačno došli smo do 111 članaka. Rezultati iz članaka iz različitih baza podataka pokazali su konzistentne rezultate imajući u vidu faktore rizika za BRONJ. Faktore rizika za razvoj BRONJ predstavljaju ekstrakcija zuba, amputacija korena, imunosupresivna terapija, viskoe doze bisfosfonata i dugotrajnost terapije (≥8 meseci)[1,2]. Oralno hirurške intervencije bi trebalo odložiti kod pacijenta sa karcinomom na terapiji visokim dozama bisfosfonata sa trajanjem terapije (≥8 meseci)[3,4]. Ukoliko to nije moguće, preporučuje se primena visokih doza antibiotika i primarno ušivanje rane. Ekstrakciju zuba ne treba pod obavezno odlagati kod pacijenata sa karcinomom na terapiji visokim dozama bisfosfonata, tako da može biti prihvatljiva u prvih 8 meseci od početka terapije visokim dozama bisfosfonata. Efikasnost kratkoročnog prekida terapije nije potvrđena[5].

ZAKLJUČAK

Multidisciplinary approach to should be primary goal in the prevention, diagnose and therapy of BRONJ. Multidisciplinarni pristup bi trebalo da bude primarni cilj u prevenciji, dijagnozi i terapiji BRONJ.

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KLJUČNE RIJEČI: bisfosfonati, osteonekroza vilice, sigurnsot

BISPOSHPONATE RELATED OSTEONECROSIS OF THE JAW – DANGEROUS REALITY

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INTRODUCTION

Bisphosphonate-related osteonecrosis (BRONJ) of the jaw presents primarily adverse side effect of bisphosphonates, especially when used at high doses in patients with cancer and bone metasthases. Many dental procedures, such as teeth extraction, oral surgery, periodontal surgery, and resective jaw bone surgery may provoke BRONJ. It is interseting to note that BRONJ may develope primarily, even without surgical intervention.

MATERIAL AND METHODS

Systematic electronic search of available literature and selection of high-quality evidence of BRONJ was done using MEDLINE, EBSCO and SCOPUS databases using appropriate keywords and terms. We included data from clinical trials, review and case reports. Research was conducted as the following ((“bisphosphonate osteonecrosis of the jaw”[Subheading] OR (“bisphosphonates “[All Fields] AND “osteonecrosis”[All Fields]) OR “bisphosphonate osteonecrosis”[All Fields]) AND ((“prevent”[All Fields]) AND (“adverse effects”[Subheading] OR (“bisphosphonates”[All Fields] AND “jaw bone”[All Fields]) OR “bisphosphonates”[All Fields]))) AND (“medical related osteonecrosis of the jaw”[MeSH Terms])).

RESULTS

Initial search initially included 2149 scientiphic articles. We used additional filters (human studies, articles published in the past 3 years, free full text) and finally came to 111 articles. Results from articles in different databases showed consistent results regarding risk factors for BRONJ. High risk factors for development of BRONJ presented tooth extraction, root amputation, immunosuppresive therapy, high doses of bisphosponates and longer duration (≥8 months)[1,2]. Oral surgery interventions should be postponed in high dose bisphosponate cancer patients with long term duration of therapy (≥8 months)[3,4]. If it is not possible, high dose of antibiotics is recommended, as well as primary suturing of the wound. Tooth extraction should not necessarily be postponed in cancer patients receiving high-dose of bisphosponates, so tooth extraction may be acceptable during high-dose bisphosphonate therapy until 8 months after initiation. The effectiveness of a short-term drug holiday was not confirmed[5].

CONCLUSION

Multidisciplinary approach to should be primary goal in the prevention, diagnose and therapy of BRONJ. Multidisciplinarni pristup bi trebalo da bude primarni cilj u prevenciji, dijagnozi i terapiji BRONJ.

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KEY WORDS: bisphosphonate, osteonecrosis jaw, safety

UVODNO PREDAVANJE

KLINIČKA FARMACIJA U HRVATSKOJ

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S kontinuiranom praksom kliničke farmacije započelo se 1996. godine u Kliničkoj bolnici Dubrava (KBD) Zagreb, na Zavodu za kardijalnu i transplantacijsku kirurgiju Klinike za kirurgiju. Tada je pokrenut pilot-projekt "Sustav raspodjele jedinične terapije" u suradnji s *Texas Heart Institute* iz Houston-a, SAD. Pilot-projekt rezultirao je smanjenjem potrošnje lijekova i uspostavom ljekarničke skrbi za hospitalizirane pacijente [1], te se s vremenom proširio i na druge zavode i odjele Klinike za kirurgiju KBD. Klinički farmaceut je postao aktivan član zdravstvenog tima, koji u praksi provodi optimizaciju i usklađivanje farmakoterapije, te prevencijom medikacijskih pogrešaka doprinosi većoj sigurnosti pacijenata [2].

Farmaceutsko-biokemijski fakultet (FBF) Sveučilišta u Zagrebu, 1998.g. u nastavu uvodi predmet Klinička farmacija prvo kao izborni, a nekoliko godina kasnije i kao obvezni kolegij, te 2006. i predmet Farmakoterapija. 2010. g. ova se dva kolegija objedinjuju u jedan Klinička farmacija s farmakoterapijom.

Akademske godine 2010./2011. FBF pokreće poslijediplomski specijalistički studij "Klinička farmacija", u trajanju od dva semestra. Namijenjen je farmaceutima iz bolničkih i javnih ljekarni i teorijski je dio programa specijalizacije iz Kliničke farmacije – bolničko i javno ljekarništvo, koju je 2008. odobrilo Ministarstvo zdravstva Republike Hrvatske (RH).

Sekcija za kliničku farmaciju Hrvatskog farmaceutskog društva, osnovana 2012.g., organizirala je dva kongresa kliničke farmacije s međunarodnim sudjelovanjem, prvi 2014. i drugi 2017. godine u Zagrebu. To je doprinjelo boljem prepoznavanju značaja kliničke farmacije te dalo dodatan poticaj njenom razvoju u Hrvatskoj.

U sustavu zdravstva RH sada je oko 25 specijalista kliničke farmacije i isto toliko specijalizanata. Poslijediplomski specijalistički studij "Klinička farmacija" na FBF-u završilo je više od 200 farmaceuta.

Osim KBD, gdje se uz praksu kliničke farmacije provodi i istraživački rad, zasad još samo nekoliko bolnica u Hrvatskoj pruža usluge kliničkih farmaceuta. Aktivnosti kliničkih farmaceuta u javnim ljekarnama polako se uvode u dnevnu praksu, a neke od njih imaju vrijedne rezultate [3].

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KLJUČNE RIJEČI: klinička farmacija, razvoj, Hrvatska

CLINICAL PHARMACY IN CROATIA

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The continuous practice of clinical pharmacy in Croatia began in 1996 at the Dubrava Clinical Hospital (KBD) Zagreb, at the Department of Cardiac and Transplant Surgery, Surgery Clinic. At that time the pilot project "Unit Therapy Allocation System" was launched in collaboration with the Texas Heart Institute in Houston, USA. The pilot project resulted in a reduction in drug consumption and the establishment of pharmacy care for hospitalized patients [1] and eventually expanded to other departments of the KBD Surgery Clinic. The clinical pharmacist has become an active member of the healthcare team, which in practice implements optimization and alignment of pharmacotherapy and contributes to greater patient safety by preventing medication errors [2].

Faculty of Pharmacy and Biochemistry (FBF), University of Zagreb, in 1998 introduced the subject Clinical Pharmacy first as an elective, and a few years later as a compulsory course, and in 2006 also the subject Pharmacotherapy. In 2010, these two courses merge into one Clinical Pharmacy with Pharmacotherapy course.

In academic year 2010/2011 FBF a postgraduate specialist study in Clinical Pharmacy for two semesters was launched. It is intended for pharmacists from hospital and public pharmacies and is theoretically part of the specialization program in Clinical Pharmacy - Hospital and Public Pharmacy, approved in 2008 by the Ministry of Health of the Republic of Croatia (RH).

The Clinical Pharmacy Section of the Croatian Pharmaceutical Society, founded in 2012, organized two congresses of clinical pharmacy with international participation, the first in 2014 and the second in 2017 in Zagreb. This contributed to a better recognition of the importance of clinical pharmacy and provided an additional impetus to its development in Croatia.

There are now about 25 clinical pharmacy specialists in the health care system in the Republic of Croatia and many specialists. More than 200 pharmacists have completed postgraduate specialist study in Clinical Pharmacy at FBF.

In addition to KBD, where clinical pharmacy practice is being conducted, only a few hospitals in Croatia provide clinical pharmacist services. The activities of clinical pharmacists in public pharmacies are slowly being introduced into daily practice, with some of them having valuable results [3].

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KEYWORDS: clinical pharmacy, development, Croatia

UVODNO PREDAVANJE

HOMEOPATIJA – NIŠTA UNUTRA– IZNENAĐUJUĆA SNAGA

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Više od 200 godina i gotovo u cijelom svijetu širi se sljedeća teza: Homeopatija je jedan od rijetkih holističkih i koherentnih medicinskih pristupa koje koriste milioni terapeuta i laika. Kako zapravo niko ne može objasniti kako ona djeluje, učinkovitost se dokazuje u nekoliko studija i metaanaliza. Ovaj uvod objašnjava pozadinu i praksu homeopatije uz živopisne primjere, a mogao bi biti razlog koji potiče čitaoca da nauči više o ovom fascinantnom, ali nekako neobičnom sistemu liječenja.

KLJUČNE RIJEČI: Homeopatija, zakon sličnosti, potentizacija, globuli, Hahnemann

HOMEOPATHY - NOTHING IN IT - SURPRISING POWERFUL

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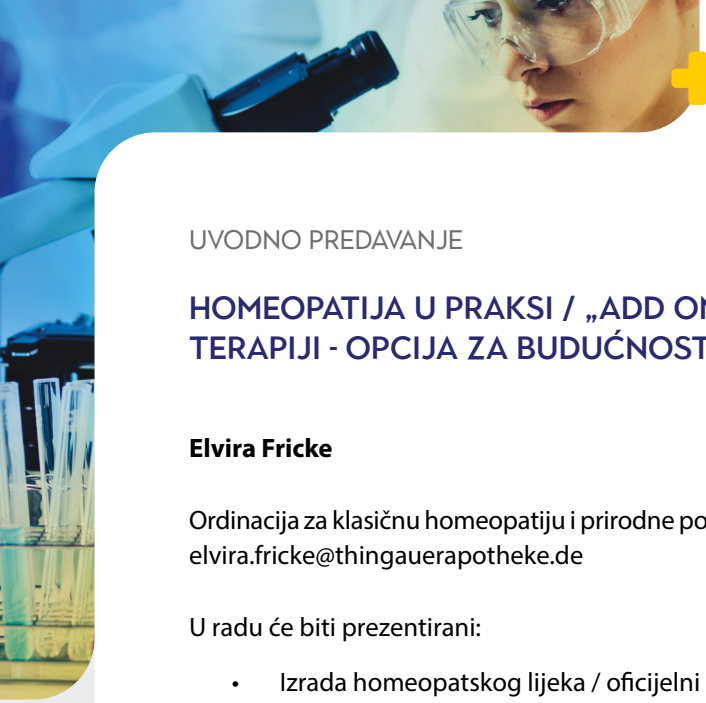
More than 200 years and nearly world-wide spread: Homeopathy is one of few holistic and coherent medical approaches used by millions of therapists and laypersons. As no-one can really explain, how it works, efficacy is proven in several studies and meta analysis. This introduction explains background and practice of homeopathy along vivid examples and could be a teaser, to learn more about this fascinating, but somehow strange therapeutic system.

KEY WORDS: Homeopathy, Law of Similarity, Potentization, Globuli, Hahnemann



UVODNO PREDAVANJE

HOMEOPATIJA U PRAKSI / „ADD ON“ KONVENCIONALNOJ MEDICINSKOJ TERAPIJI - OPCIJA ZA BUDUĆNOST?

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U radu će biti prezentirani:

- Izrada homeopatskog lijeka / oficijelni propisi / „potenciranje lijeka“
- Arnica /Hypericum / Rhus tox. / Ruta / Staphisagria / -> karakteristični simptomi ovih lijekova
- Upotreba homeopatskog lijeka i opis djelovanja / „Simile“ princip na primjeru diverse Traumata
- Izbor lijeka na osnovu simptomatike pacijenta / diferncijana dijagnosa
- Komplementerna primjena homeopatske metode / mogućnosti & granice.

Cilj primjene metode je individualizirana medicinska terapija pacijenta kao i dugoročna zdravstvena stabilnost.

HOMEOPATHY IN PRACTICE / ADD ON TO CONVENTIONAL MEDICAL THERAPY – AN OPTION FOR THE FUTURE?

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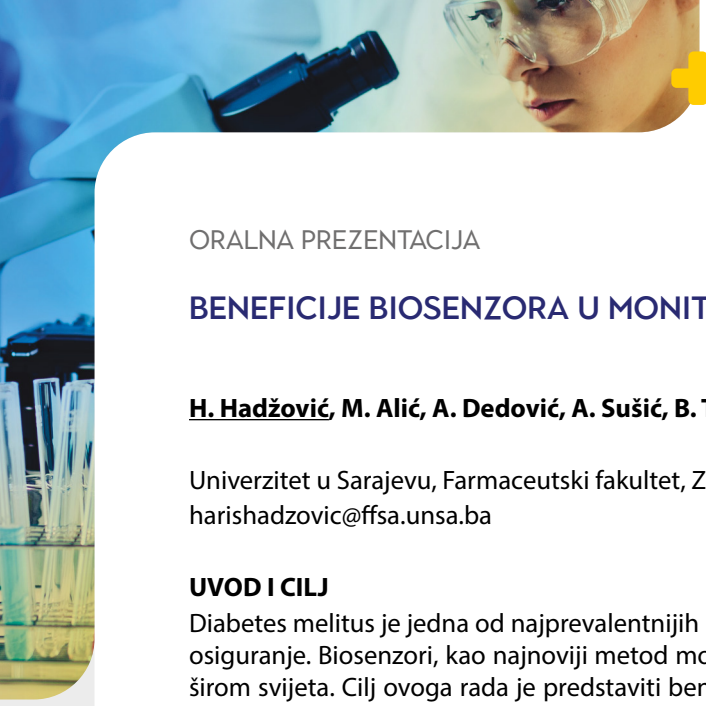
The paper presents the following:

- Preparation of homeopathic medicine / official regulations / „medicine potenting“
- Arnica /Hypericum / Rhus tox. / Ruta / Staphisagria / -> characteristic symptoms of these drugs
- Administration of homeopahtic medicine and description of its effect / Simile Principle at the example of diverse Traumata
- Selection of a medicine based on patient's symptims / differential diagnosis
- Complementary application of homeopathic method / possibilities and limitations

The aim of implementation of the method is providing an individual medical therapy to patient as well as long-term health stability.



ORALNA PREZENTACIJA

BENEFICIJE BIOSENZORA U MONITORINGU DIABETESA

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UVOD I CILJ

Diabetes melitus je jedna od najprevalentnijih bolesti u svijetu i sa sobom nosi velike troškove za zdravstveno osiguranje. Biosenzori, kao najnoviji metod monitoringa glukoze, našli su komercijalnu primjenu u zemljama širom svijeta. Cilj ovoga rada je predstaviti beneficije vezane za primjenu ovih analitičkih uređaja, a posebna pažnja je posvećena ekonomskoj isplativosti u odnosu na tradicionalni način monitoringa.

METODE

Urađena je cost-minimization analiza. Komparirali smo cijene za resurse za monitoring glukoze koristeći trandicionalni način monitoringa i biosenzore. Koristili smo više scenarija koji se odnosne na broj dnevnih mjerenja glukoze. Pored toga istraživali smo i potencijalne dodatne troškove do kojih može doći zbog lošeg monitoringa.

REZULTATI

Biosezori predstavljaju jeftiniju opciju ako broj dnevnih mjerenja premašuje 7.6. Primjećuje se smanjena incidenca teške hipoglikemije koja zahtjeva hospitalizaciju zbog poboljšanog monitoringa. Pored toga, kod korisnika tradicionalnog monitoringa u odnosu na korisnike biosenzora imamo više: hospitalizacija, dana provedenih u bolnici, poziva ambulante i odlazaka u hitnu pomoć. Svi ovi slučajevi predstavljaju dodatne troškove zdravstvenog osiguranja.

ZAKLJUČCI

Sa sigurnošću možemo tvrditi da je korištenje biosenzora opravdano i sa medicinskog i sa ekonomskog aspekta. Veći nivoi adherence se postižu sa pacijentima, što rezultira boljim titracijama inzulinskih doza. Biosenzori uopšteno poboljšavaju zdravstvenu njegu diabetesa.

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KLJUČNE RIJEČI: biosenzori, diabetes melitus, monitoring glukoze, ekonomija

BENEFITS OF USING BIOSENSORS IN DIABETIS MONITORING

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INTRODUCTION AND OBJECTIVE
Diabetes Mellitus is one of the most prevalent diseases in the world and it carries a huge economic burden for health insurance. Biosensors as a new method for glucose monitoring are being used in countries worldwide. Our objective was to present the benefits of using these analytical devices and especially cover the economic viability compared to the traditional way of glucose monitoring.

METHODS
A Cost-minimization analysis has been done. Prices for resources for glucose monitoring have been compared between traditional monitoring and biosensors. We used more scenarios which represent different numbers of daily glucose measurements. In addition, we have researched the potential additional costs that can occur as a result of poor monitoring.

RESULTS
Biosensors are cheaper if the average number of daily measurements is above 7.6. Also, there is a drop in the number of severe hypoglycemia incidences that require hospitalization because of the improved monitoring. Besides, we noticed more hospitalizations, days spent in hospital, ambulance callouts, and emergency department visits for traditional monitoring users compared to biosensor users. All of these cases represent additional health insurance costs.

CONCLUSIONS
We can safely assert that biosensor application is justified from a medical and an economic standpoint. A greater level of adherence for patients while monitoring diabetes is achieved which results in better titration of insulin doses. Biosensors overall improve health care for diabetes.

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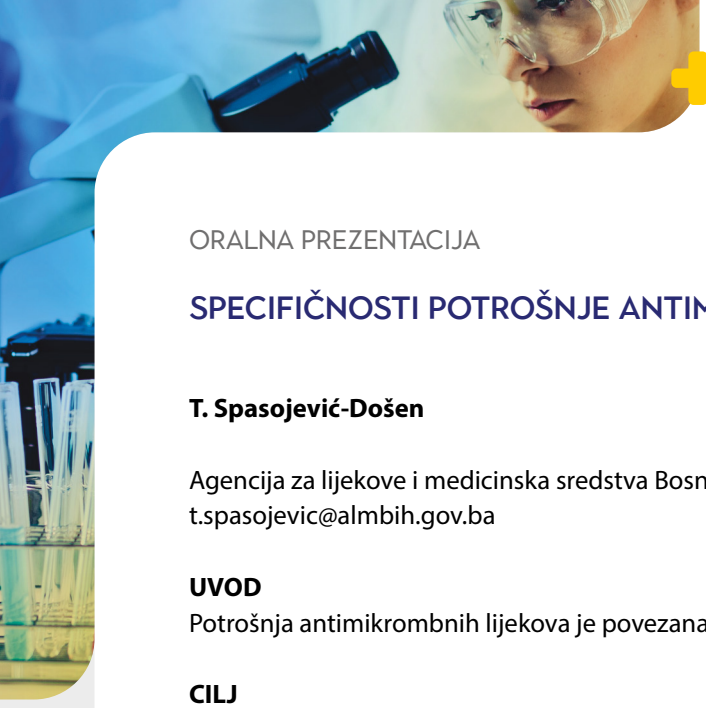
KEY WORDS: biosensors, diabetes melitus, glucose monitoring, economy



ORALNA PREZENTACIJA

SPECIFIČNOSTI POTROŠNJE ANTIMIKROBNIH LIJEKOVA U BOSNI I HERCEGOVINI

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UVOD
Potrošnja antimikrombnih lijekova je povezana sa antimikrobnom rezistencijom.

CILJ
Kontinuirano praćenje potrošnje antimikrobnih lijekova. Podaci se sakupljaju i obrađuju tako da predstavlljaju validne, reprezentativne i podatke uporedive sa podacima o potrošnji antimikrobnih lijekova u drugim državama.

MATERIJAL I METODE
Podaci o ukupnoj potrošnji antimikrobnih lijekova u Bosni i Hercegovini za period 2009-2017. su analizirani primjenom anatomsko-terapijsko-hemijskom klasifikacijom (ATC)/ definirana dnevne doza (DDD) metodologijom Svjetske zdravstvene organizacije i izraženi su u DDD/1000 stanovnika /dan (DID).

REZULTATI
Ukupna potrošnja antimikrobnih lijekova je bila 18,5 DID u 2009, 18,1 DID u 2010, 18,4 DID u 2011, 18,1 DID u 2012, 18,0 DID u 2013, 17,5 DID u 2014, 19 DID u 2015, 20,8 DID u 2016. god. i 20,3 DID u 2017. god. Prvih 5 podgrupa antibakterijskih lijekova (na trećem nivou ATC-klasifikacije) po potrošnji u 2017. god. su bili: penicilini (J01C) 10,1 DID, 49,8 % ukupne potrošnje anibakterijskih lijekova; ostali ß-laktamski antibiotici (J01D) 2,5 DID, 12,3 % ukupne potrošnje; hinoloni (J01M) 2,3 DID, 11,3 % ukupne potrošnje; makrolidi, linkozamidi i streptogramini (J01F) 2 DID, 9,9% ukupne potrošnje i sulfonamidi i trimetoprim (J01E) 1,5 DID, 7,4% ukupne potrošnje. Prvih 5 antibakterijskih lijekova po potrošnji (na petom nivou ATC-klasifikacije) u 2017. su bili: amoksicilin (4,42 DID), amoksicilin i enzim inhibitor (4,19 DID), ciprofloksacin (1,79 DID), sulfametoksazol i trimetoprim (1,52 DID) i doksiciklin (1,40 DID). Potrošnja amoksicilina i enzim inhibitora, azitromicina i ciprofloksacina se više nego udvostručila u odnosu na 2009. god.

ZAKLJUČAK
Standardizovani i validirani podaci o potrošnji antimikrobnih lijekova ukazuju na dobru propisivačku praksu (potrošnja amoksicilina) ali takođe nude mogućnost za poboljšanje (odgovarajuća upotreba amoksicilina i enzim inhibitora, azitromicina i ciprofloksacina).

KLJUČNE RIJEČI: antibiotici, potrošnja, SZO ATC/DDD metodologija, ciprofloksacin

SPECIFICITY OF ANTIMICROBIAL CONSUMPTION IN BOSNIA AND HERZEGOVINA

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INTRODUCTION
Antimicrobial consumption is associated with antimicrobial resistance.

OBJECTIVE
Continuous monitoring on antimicrobial consumption. Data is collected and processed so that shown valid, representative and comparable data with data on consumption of antimicrobial agents in other countries.

MATERIAL AND METHODS
Data on total antimicrobial consumption of Bosnia and Herzegovina for period 2009-2017 were analysed according to the WHO Anatomical Therapeutic Chemical Classification (ATC)/Defined Daily Doses (DDD) methodology and expressed in DDD/1000 inhabitants/day (DID).

RESULTS
Total (outpatients and hospital care) antimicrobial consumption was 18.5 DID in 2009, 18.1 DID in 2010 and 18.4 DID in 2011, 18,1 DID u 2012, 18,0 DID u 2013, 17,5 DID u 2014, 19 DID u 2015, 20,8 DID u 2016. god. i 20,3 DID u 2017. The top 5 antibacterial subgroups (ATC level 3) in 2017 were: penicillins (J01C) 10,1 DID, 49.8% of all antimicrobial consumption; other beta-lactam antibacterials (J01D) 2.5 DID, 12.3% of all antimicrobial consumption; quinolones (J01M) 2.3 DID, 11.3%; macrolides, lincosamides, streptogramins (J01F) 2 DID, 9,9% of all antimicrobial consumption and sulfonamides and trimethoprim (J01E) 1.5 DID, 7,4% of all antimicrobial consumption. The top 5 antibacterials (ATC level 5) in 2017 were: amoxicillin (4,42 DID), amoxicillin and enzyme inhibitor (4,19 DID), ciprofloxacin (1,79 DID), sulfomethoxazole and trimethoprim (1.52 DID) and doxycycline (1.4 DID). Consumption of amoxicillin and enzyme inhibitor, azithromycin and ciprofloxacin has more than doubled compared to 2009.

CONCLUSION
Standardized and validated data on antimicrobial consumption suggests good antibiotic prescribing practice (amoxicillin) but also offers opportunities for quality improvement (appropriate use of amoxicillin and enzyme inhibitor, azithromycin and ciprofloxacin.

KEYWORDS: antibiotics, consumption, WHO ATC/DDD methodology, ciprofloxacin

ORALNA PREZENTACIJA

ULOGA FARMACEUTA U SAVJETOVANJU O DODACIMA PREHRANI U TERAPIJI DIJABETESA

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UVOD I CILJ

Dodaci prehrani sve više se koriste kako među zdravima tako i među pacijentima sa različitim hroničnim oboljenjima. Dijabetes je pandemijsko oboljenje koje se liječi različitim intervencijama uključujući tradicionalne farmakološke terapije, ali i prirodne proizvode i dodatke prehrani (DP)[1]. Uloga farmaceuta u terapiji dijabetesa je mnogostruka i između ostalog uključuje i savjetovanje i preporuke u izboru dodataka prehrani (DP) [2,3]. Cilj našeg istraživanja bio je ispitati trenutne trendove upotrebe dodataka prehrani od strane pacijenata sa dijabetesom iz perspektive farmaceuta, stavove i poznavanje farmaceuta kada je u pitanju ova grupa proizvoda, te predložiti buduće korake vezane za ovu oblast.

METODE

Analizirali smo percepciju farmaceuta o DP koji se koriste u tretmanu dijabetesa i komplikacija korištenjem online upitnika. Upitnik je razvijen od strane autora na bazi cilja istraživanja i ranije objavljenih radova.

REZULTATI

Utvrđeno je da 73% pacijenata sa dijabetesom kupuje i koristi različite DP za koje su spremni izdvojiti 5,0-15,0 eura po jednom proizvodu. Iako u većini slučajeva farmaceuti proaktivno preporučuju ove proizvode, sami su identificirali potrebu za specijalizovanom edukacijom iz ovog područja kako bi ojačali svoje kompetencije i konkurentnost. Farmaceuti su repoznali potrebu za posebnom formulacijom DP za sniženje šećera u krvi i najčešćih komplikacija i stanja dijabetesa.

ZAKLJUČCI

Naši rezultati sugerišu da postoji rastući trend korištenja dodataka prehrani među pacijentima sa dijabetesom ali i drugim stanjima te da pacijenti žele da ih koriste uz tradicionalnu farmakološku terapiju. Farmaceuti su svjestni postojanja ovih proizvoda, ali i potrebu za postojanjem specijalizovanih formulacija za sniženje šećera u krvi i terapije najčešćih komplikacija. Dodatna edukacija posebno osmišljena za terapiju dijabetesa dodacima prehrani farmaceutima bi ojačala kompetencije i usluge koje pružaju.

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KLJUČNE RIJEČI: dodaci prehrani, dijabetes, farmaceuti, komplementarna terapija

PHARMACISTS` ROLE IN FOOD SUPPLEMENTS COUNCELING IN DIABETES TREATMENT

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INTRODUCTION AND OBJECTIVE

Food supplements utilization is showing increasing trend among healthy as well as chronic disease population. Diabetes as a pandemic disease is treated by different interventions and traditional pharmacological treatment, but also utilization of natural products and food supplements (FS) are becoming important [1]. Role of the pharmacist in diabetes management includes different interventions like counseling and recommendation of FS [2,3]. The aim of our study was to explore current trends in dietary supplements utilization among diabetic patients from the pharmacists' perspective, pharmacists' attitudes and knowledge about this group of products and suggest future directions related to this issue.

METHODS

We have analyzed pharmacists' perception of FS utilization for diabetes and its complication treatment by conducting online survey. The survey was developed by authors based on research aim and published literature.

RESULTS

It has been found that 72% of patients with diabetes are purchasing different FS and that they are willing to pay between 5,0-15,0 EUR per visit for this products. Even in majority of cases pharmacists proactively advice patients about FS selection they identify need for specific education in this field in order to strengthen their competencies and competitiveness. Pharmacists also identified need for FS specially formulated and intended for blood glucose controls and most often diabetes complications and related conditions.

CONCLUSIONS

Our findings suggest that there is a growing trend in food supplements utilization among patients with diabetes but also in other health conditions and that patient are willing to use such products as supplement to the traditional pharmacological treatments. We also found that pharmacist are aware of existence of such products but found important to have specially designed products for blood glucose reduction and supplementary treatment of mostly common diabetic complications. Additional education specially designed for diabetes treatment options and food supplements should be provided to the pharmacists in order to increase their competencies and services provided to this population.

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[3] Hughes JD, Wibowo Y, Sunderland B, Hoti K. The role of the pharmacist in the management of type 2 diabetes: current insights and future directions. Integr Pharm Res Pract. 2017;6:15-27.

KEY WORDS: dietary supplements, diabetes, pharmacists, complementary therapies

ORALNA PREZENTACIJA

GREŠKE U PROPISIVANJU LIJEKOVA U OPŠTINI VIŠEGRAD

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UVOD I CILJ
Greške u propisivanju lijekova predstavljaju problem sa kojim se suočavaju sve apoteke kao zdravstvene ustanove u BiH pa i šire. U period od 11.05.2019-11.06.2019. u ZU „Crvena apoteka“ Mrkonjić Grad, PJ „Crvena apoteka 22“ Višegrad vršeno je evidentiranje grešaka u propisivanju lijekova. Na uzorku od 2255 recepata otkrivena je 161 greška (7%).
Ovaj rad ima za cilj identifikaciju i analizu najčešćih grešaka u propisivanju i prepisivanju /transkripciji recepata u opštini Višegrad.

METODE
Praćenje i elektronska evidencija grešaka u Knjigu incidenata. Urađena je deskriptivna analiza u Exelu 2007.

REZULTATI
Evidentirane su sledeće najčešće greške u propisivanju i ispravnosti recepata i prikazan je procentualni pregled istih:

- 5 % Nedostatke pečata doma zdravlja
- 4 % Nedostatke faksimila ljekara
- 11% Nedostatak „Necesse est“
- 14 % Nedostatak signiranja (Da O.P., Da tales capsulas)
- 21 % Nedostatak broja dana za propisanu terapiju
- 15 % Propisivanje neregistrovanog lijeka
- 10% Nedostatak šifre zdravstvene ustanove sekundarnog nivoa
- 10 % Neusklađenost dijagnoze i indikacije, odnosno lijeka
- 6 % Neusklađenost participacije i kategorije oslobađanja od iste
- 2 % Lijek propisan kao privatni recept pacijentu koji ima osiguranje
- 1 % Pogrešno propisan lijek (Ibuprofen tablete za dijete od godinu dana, Dilacor ampule umjesto Dilacor tbl.)
- 1% Greške u broju dana propisane terapije
- 1% Greška u doziranju

ZAKLJUČCI
Evidentirana greška može se smatrati potencijalnim neželjenim događajem i upisana je u Knjigu incidenata koja se vodi u apoteci. Na ispravljenje ovih grešaka potrošeno je u prosjeku:

- 10 radnih sati u mjesecu koje su članovi farmaceutskog tima proveli u Domu zdravlja Višegrad
- cca 24 radna sata u mjesecu (45-60 min dnevno) farmaceutski tim izgubi na pregledanje recepata i evidentiranje grešaka u propisivanju
- Nije bilo korektivnih mjera od strane osoblja Domu Zdravlja Višegrad, po ukazivanju na greške u propisivanju.

Učestalost ponavljanja ovih grešaka smanjila bi se uvođenjem elektronskog recepata i boljom saradnjom zdravstvenih profesionalaca.

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KLJUČNE RIJEČI: greške, propisivanje lijekova

ERORRS IN PRESCRIBING MEDICINES IN THE MUNICIPALITY OF VISEGRAD/CASE STUDY

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INTRODUCTION AND OBJECTIVE

Errors in prescribing medicines are the problem that is encountered by all pharmacy stores as health institution in BiH and beyond. From 11.05.2019-11.06.2019. in ZU “ Crvena apoteka “ Mrkonjić Grad PJ “ Crvena apoteka 22”Višegrad erorrs in prescribing medicines were recorded. On the sample of 2255 recipes revealed 161 errors (7%). The aim of this paper was to identify and analyze the most common errors in prescribing and transcribing drugs prescriptions in the municipality of Višegrad.

METHODS

Monitoring and electronic logging of errors in the Book of incidents. A descriptive analysis was done in Excel 2007.

RESULTS

The following prescribing and correction errors of the recipes were recorded and a percentage review of them was shown:

- 5% lack of stamp of The Community Health Center
- 4% lack of facsimile of physician
- 11% lack of „Necesse est“
- 14% lack of „Da O.P., Da tales capsulas“
- 21% lack of days for prescribed therapy
- 15% prescribing unregistered medicines
- 10% lack of a code of a secondary level health care institution
- 10% diagnosis/ indication mismatch
- 6% inconsistency between participation and exemption category
- 2% privately prescribed recipes for insured patients
- 1% mis-prescribed medicine (Ibuprofen tablets for one year old child, Dilacor amp. instead of Dilacor tbl.)
- 1% therapy duration errors
- 1% drug dosage errors.

CONCLUSIONS

The recorded error could be considered as a potential adverse event and was recorded in the Pharmacy Book of incidents.

- For correction of these errors, the average time spent was:
- The pharmaceutical team spent 10 working hours per month tryning to corecting these errors at the Visegrad ambulance.
- The pharmaceutical team spent approximately 24 working hours per month (45-60 min per day) on reviewing prescriptions and recording prescribing errors

Prescribing errors level remained the same after corrective measures.
The frequency of recurrence of these errors could be reduced by an electronic prescription and better collaboration of healthcare professionals.

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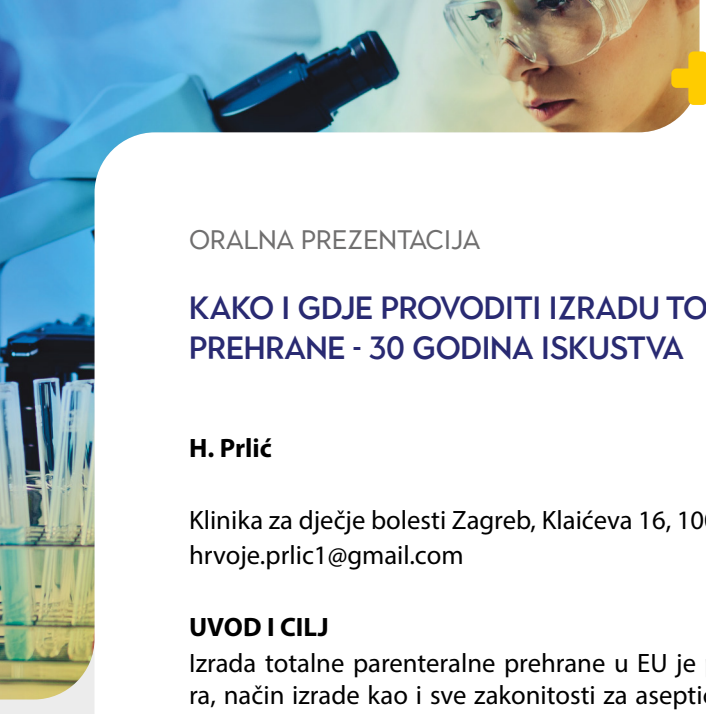
KEY WORDS: errors, prescribing drugs



ORALNA PREZENTACIJA

KAKO I GDJE PROVODITI IZRADU TOTALNE PARENTERALNE PREHRANE - 30 GODINA ISKUSTVA

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UVOD I CILJ

Izrada totalne parenteralne prehrane u EU je pokrivena brojnim smjernicama koje definiraju izgled prostora, način izrade kao i sve zakonitosti za aseptičku izradu lijekova (npr. Eudralex –The Rules Governing Medical Products in the European Union;Volume 4, EU Guidelines to GMP,ISO 9001:2000-Quality management systems-Requirements, ISO 14644-Cleanrooms and associated controlled environments...). Parenteralna prehrana se izrađuje od 1989. godine u Hrvatskom zavodu za transfuzijsku medicinu (prvo se ručno sve izrađivalo, a tijekom vremena na sve modernijim poluautomatskom i automatskim uređajima). Početkom 2015. godine u Klinici za dječje bolesti Zagreb uređen je prostor za izradu parenteralne prehrane prema svim smjernicama i jedini je prostor u RH gdje se takvi pripravci izrađuju pod nadzorom magistra farmacije.

METODE

Tako specifičan prostor zahtjeva praćenje fizikalnih i mikrobioloških parametara prema unaprijed određenim i dopuštenim granicama. Sam proces izrade totalne parenteralne prehrane je pokriven neraskidivom suradnjom liječnika, farmaceuta i medicinske sestre/roditelja koji su dio NST (eng. Nutrition support team) osnovanog još 1993. godine kao prvoga u RH.

REZULTATI

Izrada parenteralne prehrane je izuzetno specifična i opasna pa je tako u svijetu u nizu godina zabilježeno veliki broj smrtnih slučajeva povezanim sa izradom. Naša iskustva su izuzetno pozitivna i od 1989.g do danas je izrađeno više od 45000 vrećica i nije zabilježena ni jedna greška koja bi bila povezana sa izradom totalne parenteralne prehrane.

ZAKLJUČCI

Izrada parenteralne prehrane je u pogledu pogledu prostora, ljudi i svih popratnih stvari spada u najzahtjevniju izradu magistralnog pripravka i kao takva zahtjeva neraskidivu vezu između cijelog tima stručnjaka koji su dio NST-a (eng. Nutrition support team).

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[3] ISO 14644-Cleanrooms and associated controlled environments

KLJUČNE RIJEČI: totalna parenteralna prehrana,specifičan prostor, magistar farmacije, NST team

HOW AND WHERE TO MAKE TOTAL PARENTERAL NUTRITION - 30 YEARS OF EXPERIENCE

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INTRODUCTION AND OBJECTIVE

The production of total parenteral nutrition in the EU is covered by a number of guidelines that define the layout of the space, the method of manufacture and all the laws of aseptic drug manufacturing (eg Eudralex - EU Guidelines to GMP, Volume 4, EU Guidelines to GMP, ISO 9001 : 2000-Quality management systems-Requirements, ISO 14644-Cleanrooms and associated controlled environments ...). Parenteral nutrition has been made since 1989 at the Croatian Institute of Transfusion Medicine (everything was first hand-made, and over time on increasingly modern semi-automatic and automatic devices). The Paediatric Clinic Zagreb has a space for parenteral nutrition according to all guidelines and is the only space in Croatia where such preparations are made under the supervision of the Master of Pharmacy.

METHODS

Such a specific space requires monitoring of physical and microbiological parameters against predetermined and permitted limits. The whole process of making a total parental diet is covered by the unbroken cooperation of doctors, pharmacists and nurses / parents who are part of the NST (Nutrition Support Team) established back in 1993 as the first in Croatia.

RESULTS

Making a total parenteral nutrition is extremely specific and dangerous, and so many deaths have been reported in the world over the years. Our experience is extremely positive and since 1989, more than 45,000 bags have been made and any no errors have been reported that would be associated with making a total parenteral nutrition.

CONCLUSION

In terms of space, people and all related things, making parenteral nutrition is one of the most demanding preparation of a masterpiece and as such requires an unbroken link between the entire team of experts who are part of the NST (Nutrition support team).

LITERATURA

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[3] ISO 14644-Cleanrooms and associated controlled environments

KLJUČNE RIJEČI: total parenteral nutrition,specific space, Master of Pharmacy, NST team

ORALNA PREZENTACIJA

TERAPIJSKA PRIMJENA MEDICINSKIH GASOVA

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UVOD I CILJ

Medicinski gasovi su veoma specifični proizvodi namijenjeni za primjenu u medicini. Po svom agregatnom stanju i osobinama razlikuju se od svih lijekova i medicinskih sredstava dostupnih na tržištu. Uspostavljanjem novih značajnih terapeutskih postupaka, primjena medicinskih gasova se naglo povećala i postali su neizostavni dio terapije u svim granama medicine.

STATUS GASOVA ZA MEDICINSKU UPOTREBU U ZEMLJAMA EU

Status medicinskih gasova u Evropi ali i u svijetu je veoma različit- u mnogim evropskim zemljama neki gasovi spadaju u lijekove a u drugim su medicinska sredstva (CO_2 u Austriji i Srbiji je lijek, u mnogim zemljama EU je medicinsko sredstvo klase IIa; režim izdavanja O_2 u Austriji je OTC u ostalim evropskim zemljama R ili SZ).

SPECIFIČNOST MEDICINSKIH GASOVA

Gasovi koji se koriste u medicinske svrhe su po velikom broju osobina specifični – sastav, izgled (nevidljivi su), pakovanje (boca, skup boca, kontejner), doziranje, postupak proizvodnje i kontrole, primjena (gasne instalacije u bolnicama, specijalizovana medicinska sredstva), individualna primjena, itd.

TERAPIJSKA PRIMJENA MEDICINSKIH GASOVA

Azot suboksid -primjenjuje se za inhalacionu anesteziju sa drugim inhalacionim ili iv anesteticima i za analgeziju bez gubitka svijesti

Kiseonik – liječenje ili prevencija hipoksije kod: HOBP, infarkta miokarda, embolije pluća, *status asthmaticus*, akutna oboljenja pluća, trauma glave, trovanje CO2, teška anemija, lokalna ishemija tkiva itd. Koristi se u anesteziji i intenzivnoj njezi. Hiperbarični kiseonik u hiperbaričnim komorama- kod trovanja CO2, ronilačke dekompresijske bolesti, vazdušne- gasne embolije. Kiseonik se primjenjuje i u terapiji povreda i ublažavanju prirodnog starenja kože

Ugljendioksid - liječenje trovanja ugljen-monoksidom, hiperventilacija, uduvavanje pri endoskopskim zahvatima, klinička eksperimentalna i fiziološka ispitivanja, fiziko-medicinska upotreba. Sve češća je primjena u kozmetologiji u svrhu otklanjanja celulita i strija i za sprečavanje smanjenja elastičnosti kože

Azot monoksid u azotu – poboljšanje oksigenacije u liječenju novorođenčadi; smanjenje pritiska u plućnoj arteriji i poboljšanje funkcije desne komore kod plućne hipertenzije

Tečni azot – upotreba u krioterapiji, kriohirurgiji, za čuvanje biološkog materijala

U svijetu se u medicinske svrhe koriste i ksenon, helijum, argon, medicinski sintetički vazduh, *Lung Funkction Gases*. Osim brojnih terapijskih indikacija gasovi medicinskog kvaliteta imaju primjenu i u laboratorijskom radu ali i u kozmetologiji.

ZAKLJUČCI

Velika prednost medicinskih gasova je njihova jednostavna formulacija, visoka čistoća, nepostojanje degradacionih proizvoda, velika stabilnost, mali broj interakcija sa drugim lijekovima kao i neinvazivni način primjene. Primjena medicinskih gasova je izuzetno značajna a ovi specifični proizvodi su široko u upotrebi u cijelom svijetu. Od pomoćnih sredstava u medicini postali su nezaobilazni dio skoro svakog terapijskog postupka a sve je više indikacija u kojima imaju značajnu ulogu.

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KLJUČNE RIJEČI: medicinski gas, gas, terapijska primena

APPLICATION OF MEDICAL GASES IN THERAPY

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INTRODUCTION AND OBJECTIVE

Medical gases are very specific products intended for medical applications. In their aggregate condition and properties, they are different from all drugs and medicines available on the market. With the establishment of new significant therapeutic procedures, the use of medical gases has increased rapidly and they have become an indispensable part of therapy in all branches of medicine.

MEDICAL GASES SITUATION FOR MEDICAL USE IN EU COUNTRIES

The situatuon of medical gases in Europe and in the world is very different- in many European countries, some gases are drugs and others are medical devices (CO_2 in Austria and Serbia is drug, in many EU countries it is a class IIa medical device; O_2 release regime in Austria is OTC and in other European countries R or NW).

SPECIFICITY OF MEDICAL GASES

Gases used for medical purposes are specific by their many characteristics - composition, appearance (invisible), packaging (bottle, set of bottles, container), dosage, production and control process, application (gas installations in hospitals, specialized medical devices), individual application, etc.

THERAPEUTICAL APPLICATION OF MEDICAL GASES

Nitro suboxide - used for inhalation for anesthesia with other inhaled or iv anesthetics and for analgesia without loss of consciousness.
Oxygen - treatment or prevention of hypoxia in: COPD, myocardial infarction, pulmonary embolism, asthmaticus status, acute lung disease, head trauma, CO_2 poisoning, severe anemia, local tissue ischemia, etc. It is used in anesthesia and intensive care. Hyperbaric oxygen in hyperbaric chambers - CO_2 poisoning, diving decompression sickness, air-gas embolism. Oxygen is also used in the treatment of injuries and to relieve natural skin aging
Carbon dioxide - treatment of carbon monoxide poisoning, hyperventilation, endoscopic inhalation, clinical experimental and physiological tests, physico-medical use. It is increasingly used in cosmetology to eliminate cellulite and stretch marks and to prevent skin elasticity.
Nitrogen monoxide in nitrogen - improving oxygenation in the treatment of newborns; reduction of pulmonary artery pressure and improvement of right ventricular function in pulmonary hypertension
Liquid nitrogen - use in cryotherapy, cryosurgery, for preservation of biological material.
Used are also xenon, helium, argon, medical synthetic air, lung funkction gases for medical purposes. In addition to numerous therapeutic indications, medical grade gases are used in laboratory work as well as in cosmetology.

CONCLUSIONS

The great advantage of medical gases is their simple formulation, high purity, absence of degradation products, high stability, low number of interactions with other drugs as well as non-invasive method of administration. The use of medical gases is extremely important and these specific products are widely used throughout the world. Of medical aids, they have become an indispensable part of almost every therapeutic procedure and there are more and more indications in which they play a significant role.

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[3] European Industrial Gas Association (EIGA) : https://www.eiga.eu

KEY WORDS: medical gas, gas, therapeutic application

ORALNA PREZENTACIJA

MEĐUSOBNO VREDNOVANJE - BENCHMARKING APOTEKA ZASNOVANO NA INDIKATORIMA KVALITETA

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UVOD I CILJ

Ekonomski metod benchmarking se često koristi i u poređenju efikasnosti apoteka. Međutim, uloga apoteka u zdravstvenom sistemu utječe na ciljeve tih organizacija i važnost postojećeg sistema kvalitete [1]. Fokus na ishode u zdravstvu stavlja orijentaciju na pokazatelje kvalitete (QI) koji mjere kvalitetu usluga apoteka. Usporedba kvalitete usluga apoteka trebala bi biti jednostavna i vizuelna kako bi omogućila njihov razvoj i prikaz trenutačnog stanja kvalitete usluga kao i njegovo poboljšanje.

METODE

Izvršeno je mjerenje indikatora kvaliteta (QI) u 3 apoteke korištenjem IRRK metodologije [2]. Rezultati dobijeni za svaku apoteku su poravnani za svaki indikator kvaliteta (QI) i upoređeni prikazom kroz paukov dijagram.

REZULTATI

Rezultati za svaku apoteku pokazuju veliki disbalans u vrijednostima indikatora kvaliteta sa najmanjom procentualnom vrijednošću o upoznatosti ljudi sa mogućim neželjenim dejstvima propisanih lijekova (30% i niže). Relativno veći procenat prisutan je, na primjer, u slučaju poznavanja doziranja i učestalosti primjene lijeka sa više od 90%, ipak vodi u zabludu jer u apsolutnom broju i dalje predstavlja veliki broj ljudi bez razumijevanja kako tačno treba primjenjivati propisani lijek. Idealan rezultat je 100% ili točka na rubu paukovog dijagrama.

ZAKLJUČCI

Predstavljeni rezultati pokazuju da bi se objavljeni rezultati mogli upotrijebiti kao standard u branži za svaki indikator kvaliteta. Rezultati također pokazuju da bi se pristup mogao upotrijebiti za procjenu poboljšanja indikatora kvaliteta koje svaka apoteka može očekivati u usporedbi s ostalim, u realističnim uvjetima u pogledu vremena i angažiranosti. Ipak, u budućnosti bi trebalo analizirati usporedbu vrijednosti među državama kako bi se istražio utjecaj specifičnih faktora za pojedinu zemlju na standardne vrijednosti indikatora kvaliteta [3].

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KLJUČNE RIJEČI: indikatori kvalitete, medjusobno upoređivanje apoteka

COMMUNITY PHARMACY BECHMARKING BASED ON QUALITY INDICATORS

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INTRODUCTION AND OBJECTIVE

Benchmarking as a method coming from science of economic is usually used for comparison of effectiveness in Community Pharmacies (CP) as well. However, the role of CP in a healthcare system influences the goals of organizations and importance of the Quality System in place [1]. A focus on healthcare outcomes is bringing orientation on the quality indicators (QI) measuring the quality of CP services. A comparison of quality of CP services should be simple and visual to enable their development and a presentation of a current status of services quality as well as its improvement.

METHODS

QI reflecting the compliance with prescribed medicines are measured in 3 CP using IRRK methodology [2]. Each CP results are aligned for each QI and compared in spider chart diagram.

RESULTS

Results of each CP shows great imbalance in values of QI with the lowest percentage of people knowing the possible side effects of prescribed medicines (30% or below). The relatively high percentage presenting for example people knowing the prescribed dosage and frequency of administration of prescribed medicine with more than 90% are however in a way misleading since in absolute numbers they still present a high number of people without understanding how exactly they should administer the prescribed medicine. The ideal result is 100% or a point on the edge of a spider chart diagram.

CONCLUSIONS

Presented results shows the highest published results could be used as an industry standard for each QI. The results also show the approach could be used as an estimated improvement in QI each CP can expect in comparison with others in realistic terms regarding time in engagement. Nevertheless in future a comparison among countries should be analysed to investigate the influence of country specific factors on standard values of the QI [3].

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KEY WORDS: community pharmacy quality indicators, benchmarking

ORALNA PREZENTACIJA

PREGLED INDIKATORA SIGURNOSTI ZA APOTEKE NA PODRUČJU FEDERACIJE BOSNE I HERCEGOVINE ZA 2017. GODINU

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UVOD

Agencija za kvalitet i akreditaciju u zdravstvu u FBiH (AKAZ) je objavila set indikatora sigurnosti za apoteke, koji su obavezni da se dostavljaju u AKAZ [1]. Indikatori se prate u smislu unutrašnje provjere optimalnog nivoa sigurnosti pružanja zdravstvenih usluga prema Zakonu [2]. Godine 2017. su se ispunili uslovi za prikupljanje indikatora sigurnosti u apotekama, a uslovi su podrazumijevali razvoj i definisanje samih indikatora od strane radne grupe, metodologiju i vremenski raspon njihovog izračunavanja te obrazac za popunjavanje i dostavljanje u AKAZ.

METODE

Agencija za kvalitet i akreditaciju u zdravstvu u FBiH je razvila i definisala indikatore sigurnosti 2016. godine, koje su sve apoteke obavezne dostavljati kao i metodologiju za njihov izračun. Oni su integrisani i objavljeni u Standardima [3]. Agencija je prikupila rezultate indikatora od apoteka, evaluirala i komparirala rezultate indikatora sigurnosti za apoteke za 2017. godinu u ovom radu.

REZULTATI

U martu 2018. godine su 93 apoteke sa područja FBiH dostavile prvi set izračunatih indikatora sigurnosti. Podaci su prikupljani pojedinačno za svaku apoteku za 12 mjeseci prethodne godine (od januara do decembra 2017. godine), a sama analiza podataka je rađena početkom 2018. godine da bi se mogli dostaviti u traženom periodu u AKAZ (mart 2018. godine).

ZAKLJUČAK

AKAZ je prikupio, analizirao i deponovao podatke za dostavljene indikatore. Može se zaključiti da postoji veliki diverzitet u rezultatima među pojedinim apotekama neovisno o geografskom položaju. Diverzitet bi se mogao pripisati manjkavom prikupljanju podataka i pogrešnom obračunu indikatora. Imajući u vidu da je ovo prva godina prikupljanja indikatora sigurnosti za apoteke, može se smatrati velikim uspjehom broj apoteka koje su dostavile indikatore. Za tačnije rezultate je potrebno više edukacije osoblja apoteka koje radi na indikatorima kao i podrobnijem uputstvu za prikupljanje i izračun istih od strane AKAZ-a.

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KLJUČNE RIJEČI: AKAZ, indikatori, apoteke

OVERVIEW OF SAFETY INDICATORS FOR PHARMACIES IN FEDERATION OF BOSNIA AND HERZEGOVINA IN 2017

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INTRODUCTION

Agency for Healthcare Quality and Accreditation in FBiH (AKAZ) has announced set of safety indicators for pharmacies that are mandatory to be delivered to AKAZ [1]. Indicators are needed to be followed for internal assessment of optimal safety level for healthcare services according to Law [2]. In year of 2017 all conditions for collection of safety indicators in pharmacies were met. They considered development and definition of safety indicators alone, methodology and timeframe for their caluculus as well as form for reporting the results to AKAZ.

METHODS

Agency for Healthcare Quality and Accreditation in FBiH has developed and defined the safety indicators for pharmacies in 2016 that are mandatory for all pharmacies to report, as well as the methodology for their calculus. The indicators are integrated and published in Standards [3]. Agency for Healthcare Quality and Accreditation in FBiH has collected indicators results form pharmacies for 2017, as well as evaluated and compared them in this paper.

RESULTS

In March 2018 93 pharmacies from FBiH have delivered the first set of calculated safety indicators. The data were collected for evry pharmacy individually for 12 months in previous year (January to December 2017), and the calculus as well as analysis were done begin of 2018 so the data could be reported to AKAZ as requested per timeline (March 2018).

CONCLUSION

AKAZ has collected, analized and archived the data for reported safety indicators. From the overall data it can be concluded that significant diversity among results is present between single pharmacies independently of geographic position. Diversity could be due to faliures in data collection and miscalculation. Considering that this was the first year of safety indicators collection it can be considered the great success the number of pharmacies to deliver the data. On the other hand, for more accurate results more education of pharmacy staff is needed as well as more precise and detailed directions for collection and calculus of indicators from AKAZ.

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KEY WORDS: AKAZ, indicators, pharmacies

ORALNA PREZENTACIJA

ERGONOMSKI RIZICI FARMACEUTA U APOTEKAMA

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UVOD I CILJ:
Prema Međunarodnom ergonomijskom udruženju (IEA – *International Ergonomics Association*), ergonomija je znanstvena disciplina koja podrazumijeva međudjelovanje ljudi i drugih elemenata sustava, odnosno struka, koja primjenjuje teoriju, principe, podatke i metode oblikovanja sa svrhom optimiziranja dobrobiti čovjeka i općih svojstava sustava. Ergonomisti doprinose oblikovanju i vrijednovanju zadataka, poslova, proizvoda, okoliša i sustava kako bi oni postali kompatibilni s potrebama, sposobnostima i ograničenjima čovjeka. Osnovni zadatak ergonomije je prilagođavanje rada čovjeku s tri aspekta:

- prilagođavanje mašina i alata koji moraju biti projektirani tako da uvažavaju anatomske, fiziološke i psihofiziološke karakteristike čovjeka,
- prilagođavanje metoda rada čovjeku u odnosu na radne položaje i pokrete, podjelu rada, organizaciju i sredstva za rad i
- prilagođavanje uvjeta radne okoline [1].

Osnovni cilj ove studije je evaluacija ergonomskog rizika kod magistara farmacije i farmaceutskih tehničara u apotekama prilikom obavljanja različitih zadataka.

METODE:
Za evaluaciju ergonomskog rizika korištene su tri metode: OWAS [2]. (*Ovako Working posture Assessment System*), REBA [3] (*Rapid Entire Body Assessment*) i nordijski [4] upitnik. Podaci su obrađeni osnovnim deskriptivnim statističkim metodama. Statistička signifikantnost između određenih demografskih karakteristika i ergonomskog rizika je određivana neparametrijskim *Mann-Whitney U* testom.

REZULTATI:
U studiji je učestvovalo ukupno 60 ispitanika, 30 magistara farmacije i 30 farmaceutskih tehničara. Najčešće nelagode kod magistara farmacije nastaju u predjelu vrata i donjih ekstremiteta uslijed dugog stajanja za računarom pri komunikaciji sa pacijentima i obradom recepata. Kod farmaceutskih tehničara najčešće nelagode su u predjelu donjih ekstremiteta, zglobova i leđa koje nastaju uslijed nepravilnog položaja tijela za računarom, čestog i ponavljanog položaja prilikom skladištenja lijekova i rada sa magistralnim pripravcima. Rezultati OWAS i REBA metode ukazuju na određene štetne učinke radnih zadataka na koštanomišićni sistem radnika.

ZAKLJUČCI:
Neophodno je educirati magistre farmacije i farmaceutske tehničare o ergonomskim rizicima na poslu koji nastaju prilikom izvršavanja radnih zadataka. Sugerirati poslodavcima optimiziranje radne sredine u cilju minimiziranja ergonomskih rizika za uposlenike.

LITERATURA:
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KLJUČNE RIJEČI: ergonomija, rizik, koštanomišićne povrede, farmaceut.

ERGONOMIC RISKS OF PHARMACISTS IN PHARMACIES

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INTRODUCTION AND AIM: According to International Ergonomics Association (IEA), ergonomy is scientific discipline which implies interaction between people and other elements of system. It is a profession which uses theory, principles, data and designing methods to optimise the welfare of human and general features of the system. Ergonomists are contributing to design and value of tasks, jobs, products, environment and systems so they can be compatible with needs, abilities and limitations of human. The main task of ergonomy is adjustment of work to human in three aspects:

- adjustment of machines and tools which should be projected according to human anatomy, physical and pyschophysiological characteristics,
- adjustment methods of work to human according to working postures and movements, organisation and tools for work and
- adjustment of working environment conditions [1].

The main aim of this study was evaluation of ergonomic risks to which are exposed masters of pharmacy and pharmaceutical technicians in pharmacies through completing different working tasks.

METHODS: there were used three methods to evaluate ergonomic risk: OWAS [2] (Ovako Working posture Assessment System), REBA [3] (Rapid Entire Body Assessment) and nordic [4] questionnaire. Data were analysed with basic descriptive statistical methods. Statistic significance between specific demographic characteristics and ergonomic risk was determined by neparametric Mann-Whitney U test.

RESULTS: in study were participating 60 subjects, 30 masters of pharmacy and 30 pharmaceutical technicians. Most common discomforts in masters of pharmacy were in neck and lower extremities due to long standing at the computer when communicating with patients and processing prescriptions. For the pharmaceutical technicians, most common discomforts were in area of lower extremities, wrists and back resulting from improper working posture at the computer, common and repeated working postures during storage of drugs and work with magisterial preparations.

CONCLUSIONS: education of pharmacists about ergonomic risks at work is recommended. According to possibilities of employers, they should optimise working environment to reduce the ergonomic risks for their workers.

LITERATURE:

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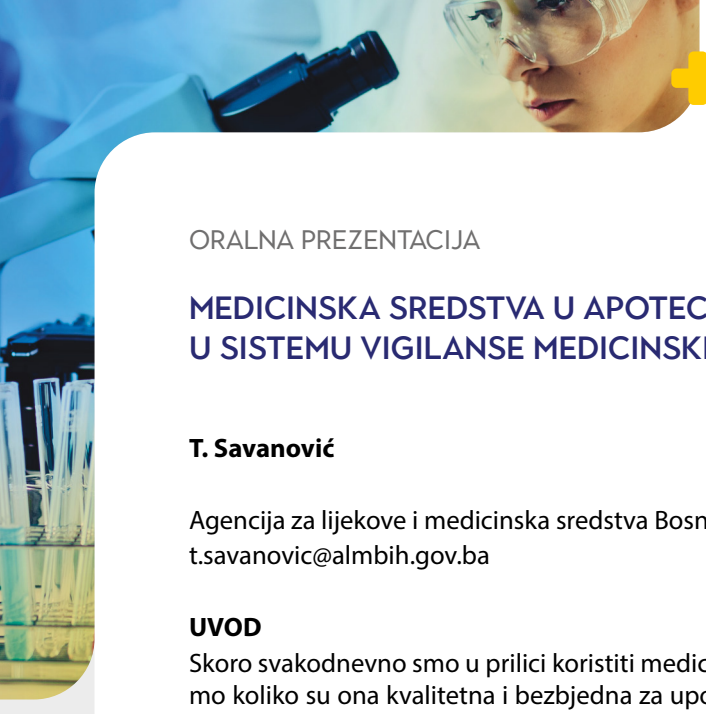
[3].Hignett S, Mcatamney L. Rapid entire body assessment (REBA). Applied Ergonomics. 2000; 31(2): 201-5.
[4].Lopez-Aragon L, Lopez-Lirisa R, Callejon-Ferre AJ, Gomez-Galan M. Applications of the standardized Nordic questionnaire: a review. Sustainability. 2017; 9(9): 1514.

KEY WORDS: ergonomy, risk, skeletomuscles injuries, pharmacist.



ORALNA PREZENTACIJA

MEDICINSKA SREDSTVA U APOTECI - ULOGA I ZNAČAJ ZDRAVSTVENIH RADNIKA U SISTEMU VIGILANSE MEDICINSKIH SREDSTAVA

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UVOD

Skoro svakodnevno smo u prilici koristiti medicinska sredstva, bilo na radnom mjestu ili u kući, a da li se upitamo koliko su ona kvalitetna i bezbjedna za upotrebu? Cilj svake zemalje je obezbjediti kvalitetna i bezbjedna medicinska sredstva neophodna za liječenje stanovništva. Svakako, najpouzdaniji način za to je praćenje medicinskog sredstva na tržištu, postmarketinška kontrola, i prijavljivanje neželjenih pojava vezanih za medicinska sredstva. U samoj postmarketinškoj kontroli medicinskog sredstva veoma važnu ulogu imaju zdravstveni radnici. Svi zdravstveni radnici moraju znati da je praćenje i prijavljivanje neželjenih pojava naša moralna, profesionalna, ali i zakonska obaveza. Osnovna svrha sistema prijavljivanja i praćenja neželjenih dejstava - vigilanse medicinskih sredstava, jeste poboljšanje zaštite zdravlja i sigurnosti pacijenta ili drugih korisnika medicinskih sredstava, kako bi se smanjila vjerovatnoća ponavljanja neželjenih pojava.

CILJ

Pojasniti sve veći značaj medicinskih sredstava koja su predmet upotrebe u svakodnevnom životu, naročito onih koji se mogu naći u apotekama, i skrenuti pažnju na značaj zdravstvenih radnika u sistemu vigilanse medicinskih sredstava.

METODE

Analiza prijavljenih slučajeva u sistemu vigilanse medicinskih sredstava i zastupljenost zdravstvenih radnika u tome, te analiza upoznatosti farmaceuta o medicinskim sredstvima u apoteci, kroz postupak akreditacije apoteka.

REZULTATI

Broj prijava neželjenih dejstava medicinskih sredstava je uopšteno mali i jako je mali procenat učešća zdravstvenih radnika u tome. Prilikom postupka akreditacije apoteka često postavljanja pitanja su šta se od medicinskih sredstava nalazi u apotekama, kako moraju biti obilježeni i da li moraju imati uputstvo za upotrebu i kako ih prepoznati?

ZAKLJUČAK

Moralna, profesionalna, ali i zakonska obaveza svakog zdravstvenog radnika je praćenje i prijavljivanje neželjenih pojava medicinskih sredstava Agenciji za lijekove i medicinska sredstva Bosne i Hercegovine. Njihova uloga je velika, jer su u direktnom kontaktu sa pacijentima, najčešćim korisnicima medicinskih sredstava. Veliki je broj medicinskih sredstava koja se mogu naći u apotekama, odnosno koja su dostupna široj javnosti. Nejasna je granica lijek-medicinsko sredstvo. Farmaceuti trebaju obratiti pažnju da li su medicinska sredstva zadovoljila Zakonom o lijekovima i medicinskim sredstvima propisane odgovarajuće kriterijume da bi se mogla naći u maloprodajnim objektima?

LITERATURA

[1] Zakona o lijekovima i medicinskim sredstvima (“Službeni glasnik BiH”, broj:58/08)
[2] Pravilnika o medicinskim sredstvima (“Službeni glasnik BiH”, broj: 4/10)
[3] Pravilnik o praćenju neželjenih pojava vezanih za medicinska sredstva (materiovigilansa medicinskih sredstava), (“Službeni glasnik Bosne i Hercegovine”, broj 58/12)

KLJUČNE RIJEČI: medicinsko sredstvo, apoteka, neželjena dejstva, zdravstveni radnici, farmaceut.

MEDICAL DEVICES IN THE PHARMACY - ROLE AND IMPORTANCE OF HEALTHCARE PROFESSIONALS IN THE SYSTEM OF VIGILANCE OF THE MEDICAL DEVICES

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INTRODUCTION

Almost every day we are able to use medical devices, whether in the workplace or at home, and do we ask ourself how good they are and safe for use? The goal of each country is to provide quality and safe medical devices necessary for the health treatments of the population. Certainly, the most reliable way to do this is to monitor medical devices on the market, post-marketing control and the report of adverse events of medical devices. Healthcare professionals have a very important role in the post-marketing control of the medical devices. All healthcare professionals need to know that monitoring and reporting of adverse events is our moral, professional and legal obligation.

THE GOAL

Explain the increasing importance of medical devices that are used in everyday life, especially those found in pharmacies, and draw attention to the importance of healthcare professionals in the medical devices vigilance system.

METHODS

Analysis of reported cases in the medical devices vigilance system and the representation of healthcare professionals in this, and analysis of pharmacists' awareness of pharmacy medical devices through the accreditation process.

THE RESULTS

The number of reports in medical devices vigilance system is small and a very small percentage of healthcare professionals participate in it.

In the accreditation proceses of pharmacy, most frequently asked questions are what of the medical devices can faund in the pharmacies, how should thay be labeled and do thay must have instructions, and how can we identify them?

CONCLUSION

The moral, professional and legal obligation of every healthcare professional is to monitor and report adverse events of medical devices to the Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina. Their role is large, because they are in direct contact with patients, the most frequent users of medical devices.

There are a large number of medical devices available in pharmacies, that is available to the general public. The boundary between medicinal products and medical devices is unclear. Pharmacists need to pay attention to whether medical devices have met the requirements of the medicinal products and medical devices act to be eligible for retail outlets?

LITERATURE

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KEY WORDS: medical devices, pharmacy, adverse events, healthcare professionals, pharmacist.

ORALNA PREZENTACIJA

ANGAŽMAN APOTEKA U BOSNI I HERCEGOVINI NA INTERNETU I DRUŠTVENIM MREŽAMA

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UVOD I CILJ

Ako zapazimo sve veće i veće prisustvo samouslužnih polica i prostora koji udaljavaju posjetioca apoteke od osobne usluge, izgleda da apoteke same ne vjeruju u dodanu vrijednost svojih usluga. Naredni korak u tom smjeru su internet apoteke [1]. U današnja vremena internet je alat koji se koristi i u apotekarskoj djelatnosti. Ovim istraživanjem cilj je bio ispitati u kojoj mjeri i na koji način apoteke u Bosni i Hercegovini koriste oglašavanja na društvenim mrežama i prodaju na internetu.

METODE

Istraživanje je, metodom opservacije, izvedeno tokom augusta 2019. godine. Napravljena je pretraga putem Google pretraživača uz prikupljanje slijedećih podataka o apotekama u BiH:

Tabela 1. *Vrsta prikupljenih podataka*

Tip zastupljenosti na internetu:	**Ispitivano:**
Internetska stranica	Prisustvo logotipa, slogana, Google Maps, Facebook biznis/privatni profil, aktivnost, tipovi objava
Facebook	
Online prodaja	

U navedenom vremenu obuhvaćeno ukupno 35 lanaca apoteka (ukupno 535 apoteka) i 48 pojedinačnih apoteka (ukupno 583 apoteke). Veličina uzorka n = 83. Lancem apoteka smatrano je tri i više jedinica. Prikupljeni podaci su predstavljeni procentualno.

REZULTATI

Tabela 2. *Rezultati istraživanja*

	DA (%)	**NE (%)**
Internetska stranica	25,30	74,70
Facebook (Facebook biznis + Facebook profil)	72,29 (60,24+12,05)	27,71
Online prodaja	4,82	95,18
Logotip	54,22	45,78
Slogan	15,66	84,34
Google maps	78,31	21,69

Aktivnost se pokazala učestalom u 25,30% slučajeva, rijetkom u 27,71% dok je ukupno neaktivnih 46,99%. Kod aktivnih 75% čine prodajne poruke, prodajne poruke praćene zdravstvenim savjetima 20,45% i 4,55% obavještenja.

ZAKLJUČCI

Zabilježeno je prisustvo 71,01% apoteka (414 od 583) sa vlastitim internet stranicama, što nam potvrđuje da apoteke u BiH koriste prednosti oglašavanja internetom.
Vrsta, frekvenca aktivnosti i broj online prodaja govore o slaboj posvećenosti ovakvom tipu promocije, a što daje nadu da je klasična briga o pacijentu u prvom planu bez obzira na izazove modernog doba.

LITERATURA

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https://covirias.eu/wp-content/uploads/2019/04/COVIRIAS_Community_Pharmacy__Advertising.pdf

KLJUČNE RIJEČI: apoteka, oglašavanje, internet

COMMUNITY PHARMACY ENGAGEMENT ON THE INTERNET AND SOCIAL MEDIA IN BOSNIA AND HERZEGOVINA

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INTRODUCTION AND OBJECTIVE

At the moment it looks like community pharmacies themselves do not believe in the added value of their services, if we acknowledge there are more and more self-service shelves and space trying to direct their visitor away from personal service. Internet pharmacy is another step in that direction [1]. Nowdays, Internet is a tool available and used even in a pharmaceutical activity. Aim of this research was to examine the extent to which community pharmacies in Bosnia and Herzegovina (B&H) use online advertising and internet sales.

METHODS

Research, using observation method, has been made during August 2019. using a Google explorer and these data about community pharmacies were collected:

Table 1. *The type of data collected*

Presence on the Internet:	Examined:
Internet page	Logotype, slogan, Google Maps, Facebook business/profil, activity, post type
Facebook profil	
Online store	

The research included 35 community pharmacy chains (535 pharmacies) and 48 single community pharmacies (583 in total). Sample size n = 83. Three and more pharmacies are considered a chain. Collected data were presented as percentage.

RESULTS

Table 2. *Results*

	YES (%)	NO (%)
Internet page	25,30	74,70
Facebook (Facebook business + Facebook profil)	72,29 (60,24+12,05)	27,71
Online store	4,82	95,18
Logotype	54,22	45,78
Slogan	15,66	84,34
Google Maps	78,31	21,69

Activity was frequent in 25,30% of pharmacies, rare in 27,71% and 46,99% showed none. 75% were sales messages, 20,45% sales messages with health advice and 4,55% were notifications.

CONCLUSIONS

Internet presence using their own websites was observed in 71.01% of pharmacies (414 out of 583), which confirm that pharmacies in B&H use the benefits of internet advertising.
The type, activity frequency and the number of online sales show poor commitment to this type of promotion, which gives hope of classic patient care at the forefront, regardless the modern age challenges.

REFERENCES

[1] Puc M. Community Pharmacy & Advertising, COVIRIAS 2017. Ljubljana 18/43
https://covirias.eu/wp-content/uploads/2019/04/COVIRIAS_Community_Pharmacy__Advertising.pdf

KEY WORDS: community pharmacy, advertising, internet

ORALNA PREZENTACIJA

PLATFORMA ZA ONLINE UČENJE

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UVOD

Sve je više kako naučnih, tako i stručnih izazova za sve zdravstvene profesionalce (magistri farmacije, doktori medicine, doktori stomatologije i drugi), te je koncept kontinuirane, cjeloživotne edukacije i usavršavanja postao izuzetno važan dio radnog procesa. Obilje novih informacija koje je potrebno usvojiti i na najbolji način iskoristiti u komunikaciji sa pacijentima, ostavlja prostora za pronalaženje novih načina za bržu i efikasniju edukaciju.

Jedan od važnijih izvora informacija u današnje vrijeme je internet. Mnoge informacije su nerecenzirane i nekvalitetne, zbog čega se gubi jako puno vremena za njihovo usvajanje.

Drugi izvori, provjerenih i kvalitetnih informacija su edukacije kroz različite vrste simpozija, kongresa i pozvanih predavanja. Ovaj vid edukacije nema mogućnost kontrole usvojenog gradiva, niti potpune interakcije između predavača i auditorija.

Navedeni nedostaci bi se mogli smanjiti, pa čak i prevazići uvođenjem platforme za online učenje. Online platforma bi trebala da omogući bolje učenje ciljane tematike. Korisnici platforme će imati mogućnost offline i online slušanja i praćenja recenziranih i precizno odabranih predavanja. Svaki od korisnika će imati svoj profil koji će koristiti za pristupanje različitim vrstama predavanja. Predavanja mogu biti raspodijeljena u nekoliko levela, radi bržeg, lakšeg i efikasnijeg praćenja. Po završetku predavanja platforma će nuditi polaganje online testa, sa pitanjima iz odslušane tematike i sa 55% i preko tačnih odgovora, može se smatrati da je korisnik uspješno odslušao predavanje iz određene oblasti.

Edukacija preko platforme pruža mogućnost edukacije na daljinu, pristupanju predavanjima u proizvoljnom vremenu i na proizvoljnoj lokaciji, preko različitih uređaja, te slušanje predavanja u različitim vremenskim intervalima, a što je najvažnije, polaganjem testa za svakog korisnika će se moći reći da je gradivo usvojeno i da je interakcija sa predavačem bila potpuna. Online platforma treba da bude pilot projekat i da edukaciju i usavršavanje zdravstvenih profesionalaca, protok znanja i novih (aktuelnih) informacija podigne na viši nivo.

KLJUČNE RIJEČI: online učenje, platforma, edukacija.

ONLINE LEARNING PLATFORM

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INTRODUCTION

There are more and more scientific and professional challenges for all health care professionals (masters of pharmacy, doctors of medicine, doctors of dentistry and others), and the concept of continuous, lifelong education and training has become an extremely important part of the work process.

A lot of new information that needs to be adopted and used to the best of our ability to communicate with patients leaves room for finding new ways to educate faster and more effectively. One of the most important sources of information these days is internet. A lot of information is unreviewed and of poor quality (low-grade quality), and because of that it takes a lot of time to preserve and adapt that knowledge. Other sources of verified and quality information are education through various types of symposia, congresses and invited lectures. This form of education does not have the ability to control adopted material, nor the complete interaction between the lecturers and the audience. These shortcomings could be reduced and even overcome by the introduction of an online learning platform. An online platform should enable better learning of targeted topics. The users of the platform will have the opportunity to listen offline and online to the peer-reviewed and precisely selected lectures. Each user will have their own profile to use to access different types of classes. Lectures can be divided into several levels for faster, easier and more efficient monitoring. After completion of the lecture, the platform will offer an online test, with 55% of the questions listened to and with correct answers, it can be considered that the user has successfully completed a lecture in a particular field.

Education through the platform gives opportunities for education on distance, to access the lectures at any time at any place over the devices. That gives the opportunity to listen to the lectures at a different time and the interaction with the lecturer is whole (complete). Learning through the online platform is intended to be a pilot project that will raise the level of knowledge of health care professionals through online educations, training and new (current) information that can be viewed in one place.

KEYWORDS: online learning, platform, education.

POSTER

UNAPREĐENJE SIGURNOSTI PRUŽANJA ZDRAVSTVENIH USLUGA U APOTEKAMA U FBIH

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UVOD

Agencija za kvalitet i akreditaciju u zdravstvu u FBiH (AKAZ) je nadležna ustanova za definisanje, prikupljanje i arhiviranje dostavljenih indikatora i izvještaja o sigurnosti i kvalitetu pružanja zdravstvenih usluga svih zdravstvenih ustanova u FBiH. Agencija je javno objavila set od pet indikatora sigurnosti za apoteke, koji su obavezni da se dostavljaju [1]. Indikatori sigurnosti [2] su namijenjeni praćenju i poboljšanju sigurnosti pružanja zdravstvenih usluga te služe kao mjerni pokazatelj istih za konkretne slučajeve.

METODE

Agencija je prikupila set od pet pojedinačnih indikatora za period 2017. (od 93 apoteke) i 2018. godinu (od 108 apoteka). Na osnovu prikupljenih rezultata indikatora sigurnosti za apoteke, urađena je evaluacija istih te komparacija prosječne veličine pokazatelja pojedinog indikatora za područje FBiH te apsolutne veličine indikatora za iste apoteke u dvije godine. Na taj način je izvršeno indirektno kompariranje sigurnosti pružanja zdravstvenih usluga u apotekama prema svih pet definisanih indikatora za 2017. i 2018. godinu.

REZULTATI

Komparacijom rezultata za 2017. i 2018. godinu uvidjelo se poboljšanje prema više pokazatelja: veći broj apoteka je dostavio rezultate indikatora, same vrijednosti indikatora pokazuju poboljšanje sigurnosti u apotekama, kako sumarno za cijelo područje FBiH tako i pojedinačno za apoteke. Jednako tako, postoji manji diverzitet rezultata apsolutnih vrijednosti indikatora među različitim apotekama prikupljenih za 2018. godinu od onih za prethodnu godinu.

ZAKLJUČAK

Nakon analize rezultata za dvije prethodne godine može se reći da je nivo sigurnosti pružanja zdravstvenih usluga u porastu u apotekama u FBiH. Apoteke su vremenom svjesnije neophodnosti izvještavanja o indikatorima sigurnosti, a iz godine u godinu su i vještije u analizi i interpretaciji rezultata dobivenih za prethodnu godinu te neophodnim akcijama za predstojeću godinu u cilju poboljšanja sigurnosti. U narednom periodu AKAZ je planirao povećati broj obaveznih indikatora koji trenutno iznosi pet na deset, kao i uvesti elektivne (izborne) indikatore koje će apoteke moći pratiti po vlastitom izboru i opredjeljenosti u poboljšanju sigurnosti pružanja zdravstvenih usluga.

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KLJUČNE RIJEČI: AKAZ, indikatori, apoteke, sigurnost

SAFETY IMPROVEMENT OF HEALTHCARE SERVICES IN PHARMACIES IN FBIH

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INTRODUCTION

Agency for Healthcare Quality and Accreditation in FBiH (AKAZ) is responsible institution for defining, collecting and archiving of reported indicators and reports for safety and quality of healthcare services in FBiH. Agency has publicly announced set of five safety indicators that are mandatory for reporting [1]. Safety indicators [2] are meant for tracking of as well as improvement of safety of healthcare services and also serve as measurable pointer in particular cases.

METHODS

Agency has collected the set of five indicators for five specific indicators for period 2017 (93 pharmacies) and 2018 (from 108 pharmacies). Based on reported results of safety indicators for pharmacies, the evaluation was done and comparation on average value of single indicator for FBiH area as well as apsolute indicator value for same pharmacies in two years. That way, indirect comparison of safety of healthcare sevices in pharmacies was done according to all five safety indicators in 2017 and 2018.

RESULTS

Comparation of results in 2017 and 2018 showed improvement according to more points: higher number of pharmacies reported the indicators results, the single values of indicators show safety improvement, as for FBiH area as for single pharmacies. Equally, the diversity of apsolute value of indicators is smaller among various pharmacies collected for 2018 than for previous year.

CONCLUSION

Following the result analysis for last two years, it can be stated that level of safety of healthcare services is rising in pharmacies in FBiH. With the time, pharmacies are more aware of necessity for reporting safety indicators, and as the time passes pharmacie staff is more skilled in analysis and interpretation of given results and needed actions for next year for safety improvment. AKAZ has planned in next period to increase the number of mandatory indicators from five to ten, as well as to introduce elective indicators that will be chosen from pharmacies to selectively monitor improvment of safety of healthcare services.

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[1] http://www.akaz.ba/udoc/Standardi20za20Apoteke202017.pdf
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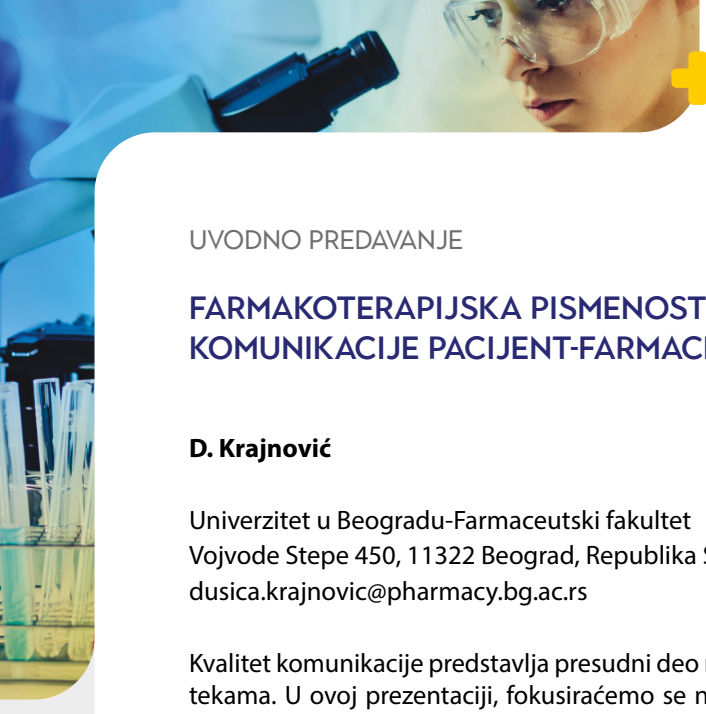
KEY WORDS: AKAZ, indicators, pharmacies, safety

SOCIJALNA FARMACIJA I ZAKONODAVSTVO

SOCIAL PHARMACY AND LEGISLATION



UVODNO PREDAVANJE

FARMAKOTERAPIJSKA PISMENOST PACIJENATA I NJEN ZNAČAJ U POBOLJŠANJU KOMUNIKACIJE PACIJENT-FARMACEUT

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Kvalitet komunikacije predstavlja presudni deo mnogih usluga u okruženju zdravstvene zaštite, posebno u apotekama. U ovoj prezentaciji, fokusiraćemo se na komunikaciju usmerenu na pacijenta. Prezentacija će početi elementima komunikacije između pacijenta i farmaceuta u kontekstu razumevanja, pronalaženja i korišćenja informacija o njihovim lekovima. Poznato je da je zdravstvena pismenost zavisna od konteksta, i u uslovima apoteke može značajno uticati na bezbednu i efektivnu upotrebu lekova [1]. Niska zdravstvena pismenost može podrazumevati pogrešno razumevanje napisanih instrukcija o lekovima, neadekvatnu adherencu prema propisanom režimu doziranja, i nemogućnost da se isprati savet zdravstvenih profesionalaca u vezi sa neželjenim efektima i mogućim kontraindikacijama. Prezentacija će ispitati neke specifične tehnologije za razvoj komunikacije pacijent-farmaceut, kao npr. kratki pregled informacija o leku, piktograme i alate za farmakoterapiju. Prezentacija će istražiti važnost farmakoterapijske pismenosti kao sposobnosti pojedinaca da pronađe, proceni, izračuna i razume pouzdane informacije u vezi sa farmakoterapijom i uslugama koje se odnose na lekove a potrebne su da bi se donele odgovarajuće odluke o upotrebi leka, bez obzira na način prenosa i sadržaj informacije (pisana, izgovorena informacija, slika ili simbol) i time smanjio rizik od loših ishoda farmakoterapije [1].

Na kraju, završiće se sa rezultatima iz farmaceutske prakse, koji pokazuju da su ograničenja u razumevanju uobičajenih informacija, široko rasprostranjena među roditeljima predškolske dece u Srbiji. Pojedinci sa ograničenom zdravstvenom pismenošću sreću se sa teškoćama u razumevanju oznaka na lekovima [2], ukazujući na farmakoterapijsku pismenost roditelja i njihove razlike u ruralnim i urbanim mestima stanovanja. Čak i obrazovane osobe se sreću sa problemima u razumevanju oznaka na lekovima i u uputstvima za lekove, jer ovi zadaci zahtevaju razumevanje i primenu informacija [3], uz napomenu da viši nivo obrazovanja nije dovoljan za razumevanje inofrmacija o lekovima. Farmaceuti, koji su najdostupniji zdravstveni profesionalci na primarnom nivou, trebalo bi da prepoznaju pacijente sa niskom farmakoterapijskom pismenošću i poboljšaju intervencije u komunikaciji koje su potrebne za dobru i bezbednu upotrebu lekova.

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[3] Ubavić S, Bogavac-Stanojević N, Jović-Vraneš A, Krajnović D. Understanding of information about medicines use among parents of pre-school children in Serbia: Parental pharmacotherapy literacy questionnaire (PTHL-SR). Int J Environ Res Public Health. 2018;15(5). https://doi.org/10.3390/ijerph15050977

Napomena: *Ovaj rad je delom podržan donacijom Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije, broj 41004.*

PATIENTS`PHARMACOTHERAPY LITERACY AND ITS IMPORTANCE FOR ENHANCING PATIENT-PHARMACIST COMMUNICATION

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The quality of communication is a crucial part of many services in health-care settings, especially at community pharmacies. In this presentation we shall focus on patient-centered communication. The presentation will began with the elements of the communication between patients and pharmacist, in the context of understanding, accessing and using the information about their medication. It is well known that health literacy is related to context and in the pharmacy setting, can greatly impact safe and effective use of medicines [1]. Poor health literacy may include misunderstanding of medicine written instructions, inadequate adherence to prescribed regimens, and inability to follow advice from health professionals regarding side effects and possible contraindications. The presentation will examine some specific technologies to develop patient-pharmacist communication, such as medication reviews, pictograms and pharmacotherapy tools. The presentation will explore the importance of the pharmacotherapy literacy as an individual's capacity to obtain, evaluate, calculate, and comprehend basic information about pharmacotherapy and pharmacy related services necessary to make appropriate medication-related decisions, regardless of the mode of content delivery (e.g. written, oral, visual images and symbols) in order to decrease the risk of bad outcomes of pharmacotherapy [1]. Finally, it will end up with some pharmacy practice research results, providing evidence that limitations in understanding common information about use of medicines are widespread among parents of per-school children in Serbia. Individuals with limited health literacy experience difficulties to understand drug labels [2] showing the pharmacotherapy literacy level of parents of and their differences with rural and urban places of residences. Even educated patients face problems interpreting labels and patient information leaflets, as these tasks require understanding and application of information [3], thus emphasizing that higher education is not requisite for understanding medical information. Pharmacists, who are the most available healthcare providers at community level need to recognise patients with low pharmacotherapy literacy and to enhance communication interventions needed for good and safe medication use.

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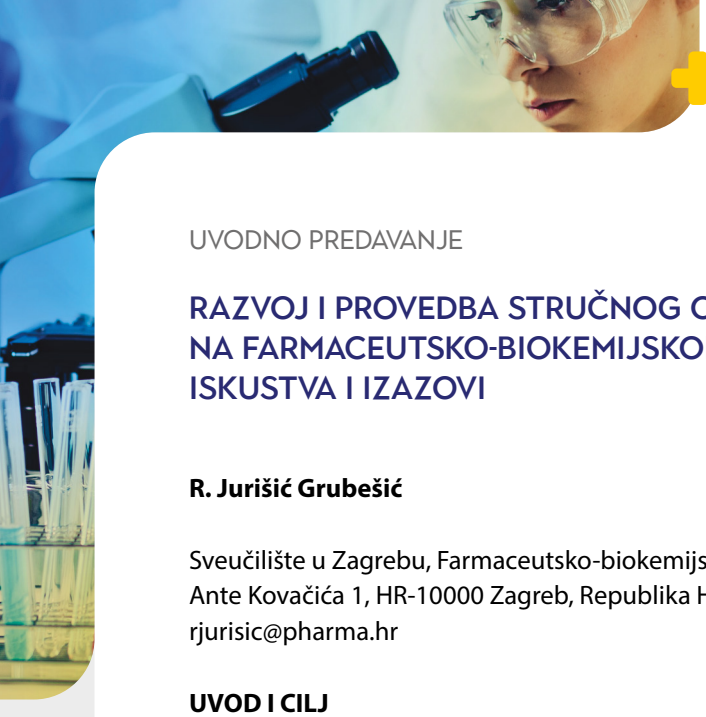
[3] Ubavić S, Bogavac-Stanojević N, Jović-Vraneš A, Krajnović D. Understanding of information about medicines use among parents of pre-school children in Serbia: Parental pharmacotherapy literacy questionnaire (PTHL-SR). Int J Environ Res Public Health. 2018;15(5). https://doi.org/10.3390/ijerph15050977



UVODNO PREDAVANJE

RAZVOJ I PROVEDBA STRUČNOG OSPOSOBLJAVANJA ZA STUDENTE FARMACIJE NA FARMACEUTSKO-BIOKEMIJSKOM FAKULTETU SVEUČILIŠTA U ZAGREBU: ISKUSTVA I IZAZOVI

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UVOD I CILJ

Obrazovanje temeljeno na kompetencijama predstavlja novu paradigmu edukacije u području biomedicine i zdravstva. Takav pristup zadobiva sve veći značaj i temelj je razvoja stručnog osposobljavanja za studente farmacije (SOF) na Farmaceutsko-biokemijskom fakultetu Sveučilišta u Zagrebu (FBF) [1]. SOF obuhvaća stručne prakse 3.-5. godine integriranog studija farmacije FBF-a te ima ključnu važnost u pripremi studenata za stjecanje znanja i tehničko-manipulativnih vještina potrebnih u ljekarničkoj praksi, a koje definira nacionalni kompetencijski okvir (HLJKO) [2]. Za uspješnu provedbu kompleksnih aktivnosti SOF-a, moraju biti zadovoljene sljedeće pretpostavke: (1) sustavna i kontinuirana edukacija nastavnika, mentora i ostalog uključenog kadra; (2) odgovarajuće prateće stručne službe za potporu studentima na SOF-u te u razvoju njihovih karijera; (3) adekvatna opremljenost vježbaonica u funkciji SOF-a; (4) suvremeni edukacijski alati za SOF; (5) ravnomjerna distribucija mentorskih baza diljem nacionalnog teritorija i (6) proširena uloga poslodavaca/mentora u realizaciji SOF-a.

METODE

Za razvoj i provedbu stručne prakse izvan visokog učilišta, odgovoran je educirani kadar Centra za primijenjenu farmaciju FBF-a (CPF). Glavne vezane aktivnosti CPF-a su: (a) razvoj modela stručne prakse, (b) educiranje uključenog kadra, (c) unapređenje sustava mentorstva i stručne prakse, (d) širenje suradnje s poslodavcima kroz partnerski odnos u provedbi SOF-a, e) koordiniranje svih dionika i aktivnosti na SOF-u.

REZULTATI

Budući da se SOF pretežno provodi u Zagrebu i okolici, a osjetan je deficit ljekarnika u ostalim dijelovima RH, CPF potiče osnivanje mentorskih baza izvan Zagreba kroz ciljane edukacije postojećih i novih mentora na SOF-u. CPF istovremeno razvija i kontinuirano unapređuje instrumente procjene uspješnosti SOF-a i stečenih vezanih kompetencija.
Aktivnosti CPF-a osiguravaju racionalnu provedbu SOF-a kroz dinamičnu interakciju svih dionika.

ZAKLJUČCI

Učenjem u praksi, studentima se omogućava šire profesionalno profiliranje te bolja usklađenost njihovih stručnih kvalifikacija s potrebama suvremenog tržišta rada. Time se ujedno potiče ravnomjernija distribucija zapošljavanja, što u konačnici povećava dostupnost i kvalitetu ljekarničkih usluga te ima pozitivan utjecaj na zdravstveni sustav u cjelini.

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KLJUČNE RIJEČI: obrazovanje temeljeno na kompetencijama, stručno osposobljavanje za studente farmacije

DEVELOPMENT AND IMPLEMENTATION OF THE PRE-REGISTRATION TRAINING FOR PHARMACY STUDENTS AT THE UNIVERSITY OF ZAGREB FACULTY OF PHARMACY AND BIOCHEMISTRY: EXPERIENCES AND CHALLENGES

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INTRODUCTION AND OBJECTIVE

Competency-based education becomes increasingly important in modern education of health professionals and is the basis of the pre-registration Professional Training for Pharmacists (PTP) at the Faculty of Pharmacy and Biochemistry (FPB), University of Zagreb, Croatia [1].

PTP encompasses professional practices on the 3rd, 4th and 5th year of the integrated study programme of Pharmacy and is of crucial importance in preparing students for the acquisition of knowledge and technical-manipulative skills required in pharmacy practice, defined by the *Croatian Competency Framework* [2]. For the successful implementation of related complex activities, the following assumptions must be met: (1) systematic and continuous education of all stakeholders; (2) appropriate support services for students at PTP; (3) adequate equipment in the function of PTP; (4) modern educational tools for PTP; (5) equal distribution of mentoring bases throughout the national territory; and (6) the extended role of employers in the realization of PTP.

METHODS

For the implementation of professional practice outside the faculty, the Centre for Applied Pharmacy (CAP) is established at the FPB. The main related activities of the CAP are: (a) developing models of pharmacy practice, (b) educating staff involved, (c) improving mentoring system, (d) expanding cooperation with employers as partners in the implementation of PTP, e) coordinating all activities on PTP.

RESULTS

PTP is predominantly carried out in Zagreb and its surroundings but the CAP strongly encourages the establishment of mentoring bases all over Croatia, especially in regions where there is a deficit of pharmacists. The CAP also develops and continuously improves assessment tools for PTP and acquired competencies. All CAP activities ensure rational implementation of PTP through the dynamic interaction of all stakeholders.

CONCLUSIONS

By learning in practice, students gain the opportunity of broader professional profiling and better aligning their qualifications with the needs of the modern labor market. PTP also contributes to the balanced distribution of pharmacists in Croatia. This ultimately increases the availability and quality of pharmacy services and has a positive impact on the healthcare system as a whole.

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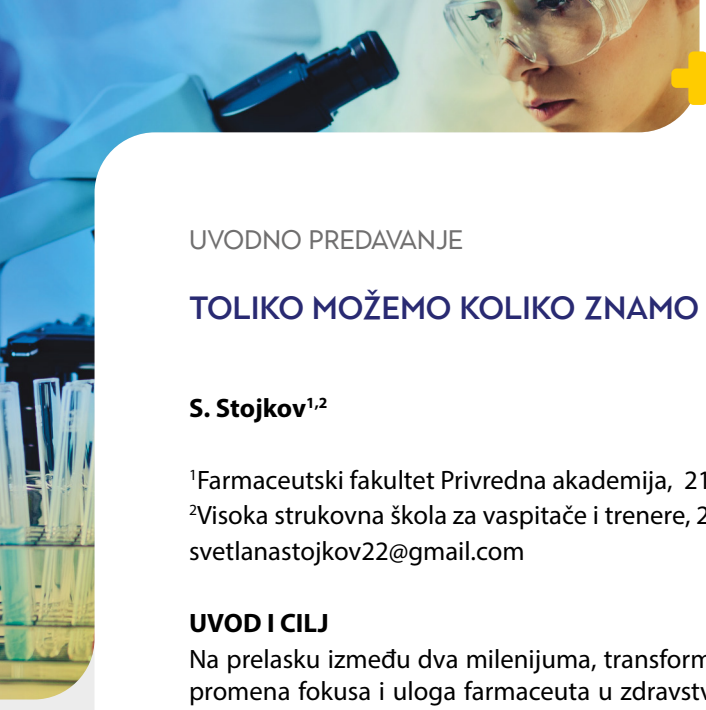
KEY WORDS: competency-based education, pre-registration training for pharmacy students



UVODNO PREDAVANJE

TOLIKO MOŽEMO KOLIKO ZNAMO – ISTINA ILI IZAZOV?

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UVOD I CILJ

Na prelasku između dva milenijuma, transformacija izazova koji su se našli pred farmaceutskom profesijom, promena fokusa i uloga farmaceuta u zdravstvenoj zaštiti, mogla bi se nazvati (r)evolucijom. Izazovi koji se postavljaju pred farmaceutski esnaf zahtevaju individualan i sistemski pristup baziran na celoživotnom učenju. Celoživotni profesionalni razvoj je u korelaciji sa kompetencijama [1] i motivacijom farmaceuta. Cilj ovog rada je istražiti motivacioni efekat unutrašnjih i spoljašnjih faktora motivacije i okvira kompetencija.

METODE

Studijom preseka izvršeno je istraživanje putem ankete dostupne na na sajtu Farmaceutske komore Srbije (FKS). Upitnik je kreiran za potrebe ovog istraživanja. Popunjavanjem upitnika farmaceuti su dali demografske podatke i iskazali stepen slaganja sa izjavama u upitniku na skali od 1(ne slažem se), 2 (uglavnom se ne slažem), 3 (nisam siguran/a), 4 (uglavnom se slažem) do 5 (slažem se u potpunosti). Statistička obrada podataka izvršena korišćenjem programa the Statistical Package for Social Sciences, verzija 22.

REZULTATI

Upitnik je popunilo 490 farmaceuta, oko 8% članova FKS u početnoj tačci istraživanja (2015.), 89% ženskog i 11% muškog pola. Godine radnog staža kretale su se od 1 do 40 godina, prosečno 15,17 godina. Najsnažniji uticaj (5) unutrašnjih faktora motivacije kretao se od 25,92% (poštovanje u timu i zajednici) do 77,96% (odgovornost u zdravstvenoj zaštiti), dok se kod spoljašnjih faktora kretao od 21,06% (veća zarada) do 26,53% (napredovanje u karijeri). Najviši stepen slaganja sa izjavom " Okvir kompetencija me je podstakao da aktivno upravljam svojim profesionalnim razvojem " iskazalo je više od polovine ispitanika [2].

ZAKLJUČCI

Motivacija zdravstvenih profesionalaca podržava neprestano ažuriranje i sticanje novih znanja i veština, važnih za sprovođenje efikasne i kvalitetne zdravstvene zaštite. Iako se ovim pitanjima bave svetski stručni autoriteti, ključna uloga je na nivou pojedinca i strukovnih organizacija.

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KLJUČNE REČI: celoživotni profesionalni razvoj, unutrašnji i spoljašnji faktori motivacije, okviri kompetencija

KNOWLEDGE IS POWER - TRUTH OR CHALLENGE?

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INTRODUCTION AND OBJECTIVE

At the turn of the millennium the transformational challenges that were set before the pharmaceutical profession, its change of focus and the role of the pharmacist within the healthcare system could be referred to as (r)evolutionary. The challenges facing the pharmaceutical guild require an individual and systemic approach, based on lifelong learning. Continuing professional development correlate with the competency [1] and motivation of the pharmacist. The objective of this paper is to research the motivational effect of internal and external motivational factors and the competency framework.

METHOD

A cross-sectional study was conducted in order to complete this research via survey available on the website of the Pharmaceutical Chamber of Serbia (FKS). A questionnaire was created specifically for the needs of this research. By filling in the questionnaire, pharmacists provided their demographic information and expressed to what level they agree with the statements made in the questionnaire on a scale from 1 (Disagree), 2 (Mostly disagree), 3 (Unsure), 4 (Mostly agree), to 5 (Strongly agree). The statistical processing of data was conducted using the programme: Statistical Package for Social Sciences, version 22.

RESULTS

The questionnaire was completed by 490 pharmacists, approx. 8% of which are members of the FKS at the starting point of the research (2015), of which 89% were women and 11% men. The number of years of service ranged from 1 to 40 years, the average being 15.17 years of service. The most impact (5) in terms of internal motivational factors ranged from 25.92% (feeling that they are a respected member of the team and community) to 77.96% (feeling responsibility toward healthcare), while the external factors ranged from 21.06% (higher salary) to 26.53% (climbing the career ladder). More than half of those surveyed answered 5 - Strongly agree with the statement "The competency framework has encouraged me to actively manage my professional development." [2]

CONCLUSION

The motivation of healthcare professionals allows for the updating and gaining of new knowledge and skills, vital to the implementation of efficient and quality healthcare. Despite the fact that this issue is being addressed by world-class expert authorities, a key role is played by the individual and by professional organisations.

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KEY WORDS: continuing professional development, internal and external motivational factors, competency framework

UVODNO PREDAVANJE

ZNAČAJ KOLABORATIVNE PRAKSE U PROCESU DONOŠENJA ODLUKA O FARMAKOTERAPIJI

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UVOD I CILJ

U cilju unapređenja kvaliteta zdravstvenih ishoda, u svetu se sve više objavljuju naučni radovi, regulatorni propisi i profesionalni vodiči u kojima se za odgovornost o propisanoj terapiji uključuje i pacijent. Cilj ovog rada je prikaz modela za donošenje odluka u farmaceutskoj kolaborativnoj praksi, u kojima će se postići autonomija farmaceuta uz poštovanje i uključivanja pacijenata u izbore vezane za njihovo zdravlje.

METODE

U cilju definisanja najboljeg modela zajedničkog odlučivanja u zdravstvenoj zaštiti, urađena je komparativna analiza svetskih vodiča ministarstva zdravlja.

Takođe, rađena je i analiza sadržaja kompjuterskih programa i mobilnih aplikacija, koje se koriste u procesu donošenja odluke.

REZULTATI

Zajedničko odlučivanje predstavlja model kolaborativne prakse u kom se donošenje odluka delegira, deli i prepliće u svim smerovima tradicionalnog lanca vrednosti [1].

Međutim, u procesu zajedničkog odlučivanja, postoje barijere, kako od strane zdravstvenih profesionalaca, tako i od strane pacijenata.

Najzastupljeniji model zajedničkog odlučivanja je IP-SDM *(Interprofessional shared decision model)*. Prema tom modelu se pacijenti ohrabruju u procesu zajedničkog odlučivanja o terapiji.

Kompjuterski program o zajedničkom odlučivanju, koji se najčešće koristi u zdravstvenoj zaštiti je AHP (Analytical Hierarchy Process) [2].

ZAKLJUČCI

Usvajanje novih tehnike i modela zdravstvene zaštite će svakako unaprediti komunikaciju između zdravstvenih profesionalaca i pacijenata, a samim tim povećati kvalitet zdravstvene zaštite.

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KLJUČNE REČI: farmaceutska kolaborativna praksa, donošenje odluka, zajedničko odlučivanje

THE IMPORTANCE OF THE COLLABORATIVE PRACTICE IN THE PROCESS OF DECISION MAKING ABOUT PHARMACOTHERAPY

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INTRODUCTION AND OBJECTIVE

In order to improve the quality of health outcomes, worldwide scientific papers, regulatory regulations and professional guides are published in which a patient is included in the responsibility for prescribed therapy. The aim of this paper is to present models for decision-making in pharmaceutical collaborative practice, in which the autonomy of pharmacist will be achieved with the respect and inclusion of patients in health-related choices.

METHODS

In order to define the best model for shared decision-making in health care, a comparative analysis of the World Health Care Guides was conducted.

Also, an analysis of the content of computer programs and mobile applications, which are used in the decision-making process, was made.

THE RESULTS

Shared decision-making is a model of collaborative practice in which decision-making is delegated, shared and interlaced in all directions of the traditional value chain [1].

However, in the process of shared decision-making, there are barriers, both by health professionals and by patients.

The most common decision-making model is IP-SDM (Inter professional shared decision model). According to this model, patients are encouraged in the process of shared decision-making on therapy.

The Computer Decision-Making Computer, commonly used in health care, is the AHP (Analytical Hierarchy Process) [2].

CONCLUSIONS

Adopting new techniques and models of health care will certainly improve communication between health professionals and patients, and thus increase the quality of health care.

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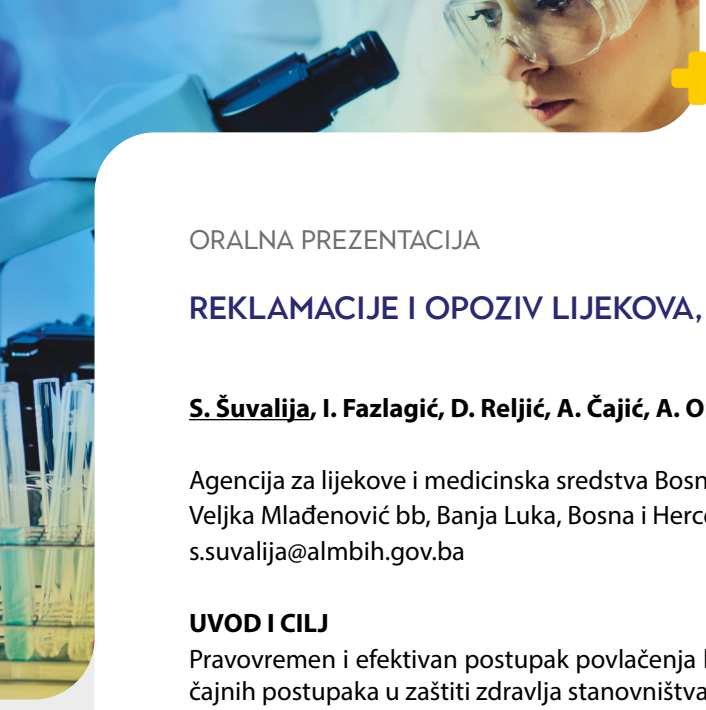
KEY WORDS: pharmacy collaborative practice, decision-making, shared decision-making



ORALNA PREZENTACIJA

REKLAMACIJE I OPOZIV LIJEKOVA, ULOGA APOTEKE U LANCU DISTRIBUCIJE

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UVOD I CILJ

Pravovremen i efektivan postupak povlačenja lijeka/ serije lijeka kroz cijeli lanac distribucije, jedan je od značajnih postupaka u zaštiti zdravlja stanovništva Bosne i Hercegovine.
Cilj rada je bio procijeniti postupanje apoteke kao posljednje karike u lancu distribucije, u postupku reklamacija i opoziva lijeka/ serije lijeka, odnosno njenu educiranost u skladu sa zakonski propisanom obavezom i odgovornošću.

METODE

Ispitivanje je provedeno u periodu 2018-2019. godina, tokom redovnog inspekcijskog nadzora nad postupanjem veleprometnika lijekovima, vezanim za reklamacije i povlačenje serija lijekova. Zasnovano je na pregledu dokumentacije evidencije veleprometnika o isporučenim i od apoteka vraćenim količinama reklamirane, odnosno povučene serije lijeka.

REZULTATI

Rezultati su zasnovani na dokumentaciji evidencije tri veleprometnika koji su prometovali sa 34 apoteke. Utvrđene su određene nepravilnosti, među kojima je evidentirano: da su lijekovi vraćeni iz apoteke u koju nisu bili isporučeni, odnosno utvrđen je promet lijekovima unutar jednog lanca apoteka, da je apoteka izdajući pacijentu ampule na komad narušila integritet pakovanja, čime je onemogućen tačan uvid u identitet pacijenta kojem je lijek izdat, te da apoteka nije direktno, fizički učestvovala u postupku povlačenja lijeka koji je isporučila zdravstvenoj ustanovi. Dobijeni rezultati su pokazali da je u većini slučajeva postupanje apoteka pravovremeno i efektivno, ali da u pojedinim slučajevima apoteke ne upravljaju reklamacijama i postupcima povlačenja na način koji osigurava zaštitu zdravlja pacijenata.

ZAKLJUČCI

Provođenje dodatne educiranosti apoteka u pogledu njihove zakonski propisane obaveze i odgovornosti na području postupanja sa prijavljenim reklamacijama, odnosno zaprimljenoj obavijsti o opozivu bi dodatno doprinijelo zaštiti zdravlja BiH populacije.

LITERATURA

[1] Zakon o lijekovima i medicinskim sredstvima (Službeni glasnik BiH, broj 58/08)
[2] Pravilnik o dobroj distributivnoj praksi (GDP) lijekova za humanu upotrebu (Službeni glasnik BiH, broj 75/13)
[3] Zakon o apotekarskoj djelatnosti (Službene novine Federacije BiH, broj 40/10)
[4] Zakon o apotekarskoj djelatnosti (Službene novine RS, broj 119/08)

KLJUČNE RIJEČI: apoteka, reklamacije, povlačenje lijeka/serije lijeka

RECLAMATION AND WHITHDRAWAL OF MEDICINES, THE ROLE OF THE PHARMACY IN THE DISTRIBUTION CHAIN

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INTRODUCTION AND OBJECTIVE
Timely and effective medicines/ batch withdrawal procedure throughout the distribution chain is one of the most significant procedures in protecting Bosnia and Herzegovina's population health. The objective of the paper was to evaluate the pharmacy's acting in the process of complaints and recall of the medicines /batch as the last link in the distribution chain and needs for additional education in accordance with the legally prescribed obligation and responsibility too.

METHODS
The research was conducted during a period in 2018-2019 during the regular inspections of the wholesalers. The aim of these inspections was an insight into the activities of the wholesalers following received complaints and during the withdrawal of batches of the medicines.

RESULTS
The results are based on the documentation and records of the three major wholesalers which traded with the 34 pharmacies. Certain deficiencies were identified. There was recorded that: the medicine was not returned from pharmacy to which was delivered, but from the other one, which is part of the same chain of pharmacies, the pharmacy not returned the whole package to the wholesaler but only one ampule, indicating that the pharmacy impairs integrity of the secondary packaged medicine and finally, the pharmacy was not directly participated in the withdrawal of the medicine, which was delivered to the medical facility.
Obtained results show that in most cases the pharmacies reacted timely and in an effective way, but some pharmacies manage complaints and withdrawal on the way which does not ensure the protection of patient's health.

CONCLUSIONS
Additional education of pharmacies regarding their legally prescribed obligations and responsibilities in the area of handling and reporting of complaints and received notice of withdrawal would further contribute to the protection of population in Bosnia and Herzegovina.

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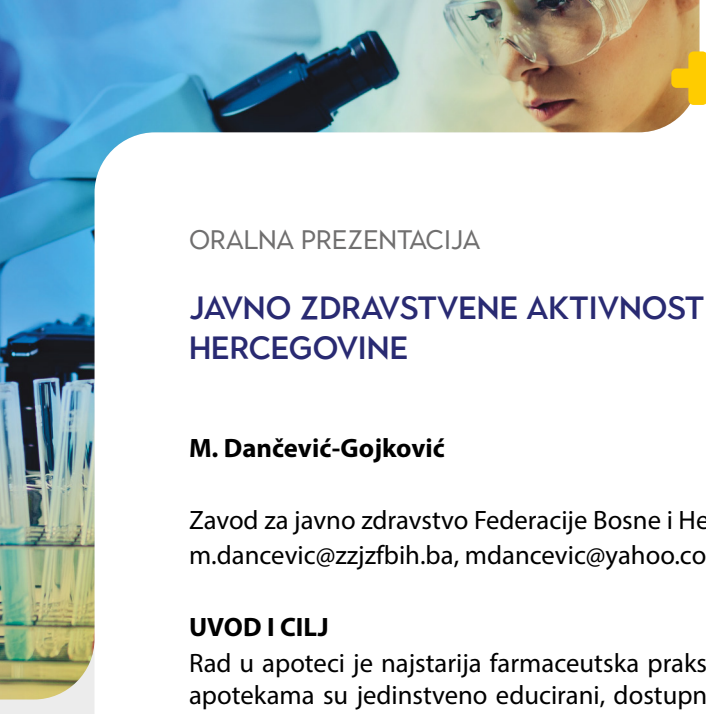
[2] Pravilnik o dobroj distributivnoj praksi (GDP) lijekova za humanu upotrebu (Službeni glasnik BiH, broj 75/13)
[3] Zakon o apotekarskoj djelatnosti (Službene novine Federacije BiH, broj 40/10)
[4] Zakon o apotekarskoj djelatnosti (Službene novine RS, broj 119/08)

KEY WORDS: pharmacy, complaints, drug withdrawal



ORALNA PREZENTACIJA

JAVNO ZDRAVSTVENE AKTIVNOSTI FARMACEUTA U FEDERACIJI BOSNE I HERCEGOVINE

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UVOD I CILJ

Rad u apoteci je najstarija farmaceutska praksa i većinom prvi izbor diplomiranih farmaceuta. Farmaceuti u apotekama su jedinstveno educirani, dostupni i pristupačni većini stanovništva, ali njihov doprinos poboljšanju zdravlja pružanjem javnih zdravstvenih usluga često nije prepoznat. Ova studija prikazuje opseg i vrste javno zdravstvenih usluga i promovisanja zdravlja u radu farmaceuta u apotekama širom FBiH.

METODE

U radu je korištena interaktivna rasprava fokus grupa nasumično odabranih učesnika tokom stažiranja u Zavodu za javno zdravstvo FBiH, radi samoprocjene farmaceutske prakse, u trajanju od 1 ± 2 sata koja istražuje specifičan skup pitanja o unaprijed određenim temama i terminima, kao što su javno zdravstvo, promocija zdravlja, zdravstvena pismenost.

REZULTATI

Rezultati su analizirani kao povratne informacije koristeći istu metodologiju u kontekstu plana i programa pripravničkog staža: prvo polaznici su bili upitani šta je za njih (u apotekarskoj praksi) javno zdravlje i promocija zdravlja, a nakon toga su imali interaktivno predavanje o aktivnosti promicanja zdravlja, sa naglaskom na komunikaciju i zdravstvenu pismenost u apotekarskoj praksi, ulogu i položaj farmaceuta u zdravstvenom sistemu u Bosni i Hercegovini, te mogućnosti interdisciplinarne interakcije i angažmana. Zbirni rezultati daju smjernice o prepoznavanju struke i budućim izazovima - iskustvu, svijesti, osnaživanju, odnosima.

ZAKLJUČCI

Ovaj rad podvlači ulogu farmaceuta koja se mijenja - ne samo kao stručnjaka za lijekove, već i kao stručnjaka za javno zdravstvo, a što je još uvijek nedovoljno prepoznato i iskorišteno u Bosni i Hercegovini. U cilju promovisanja veće učinkovitosti i sigurnosti sistema medicinske i zdravstvene zaštite, te kroz reformu zdravstvene zaštite koja je u toku, a prema međunarodnim profesionalnim zahtjevima koja važi za sve farmaceute, a posebno one na početku profesionalne karijere, treba u budućnosti podržati i poboljšanju profesionalne aktivnosti farmaceuta na jačanju njihove javno zdravstvene uloge.

KLJUČNE RIJEČI: javno zdravstvo, farmaceut, apoteka u zajednici, Bosna i Hercegovina

COMMUNITY PHARMACIST'S PUBLIC HEALTH ACTIVITIES IN FEDERATION OF BOSNIA AND HERZEGOVINA

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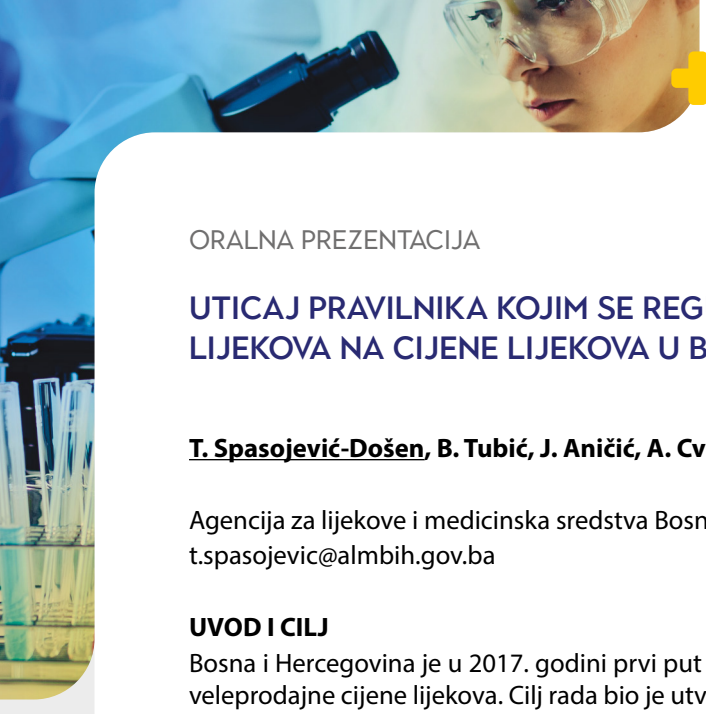
INTRODUCTION AND OBJECTIVE
The community practice is the oldest pharmacy practice, and remains the first choice of majority pharmacy graduates. Pharmacists are uniquely qualified, available and accessible to the majority of population, but their contributions to improve health through the delivery of public health services often go unrecognized This study aims to provide a picture of the extent and nature of public health and health promotion services within pharmacies across FB&H.

METHODS
Interactive focus group discussion of 1±2 hours' duration that explores a specific set of issues on a predefined and limited topics and terms as health promotion, health literacy, public health during the internship in Public Health institute FB&H to self-estimate pharmacist practice, randomly selected participants.

RESULTS
Results were analysed as the feedback using the same methodology within the context of the internship curriculum: first participants were asked what is public health and health promotion for them (in their on-going practice), and afterwards they have had an interactive lecture on the health promotion activities, pointed communication and health literacy in pharmacy practice, roles, and position of the pharmacist in the health care system in Bosnia and Herzegovina, options of interdisciplinary interaction and engagement. Aggregated results provide guidance on specific recognition and challenges for the practitioners - experience, awareness, empowerment and relationships.

CONCLUSIONS
This paper underlining the changing role of pharmacist not only as drug experts, but as the public health professionals, that is still underutilised resources in Bosnia and Herzegovina in promoting the increasing effectiveness and safety of the system of medical and health care, besides on going health reform, and internationally professional requests It is imperative for all pharmacist, but particulally novice, in maintaining and improving professional activity in the future.

KEYWORDS: Public health, Pharmacist, Community pharmacy service, Bosnia and Herzegovina



ORALNA PREZENTACIJA

UTICAJ PRAVILNIKA KOJIM SE REGULIŠU MAKSIMALNE VELEPRODAJNE CIJENE LIJEKOVA NA CIJENE LIJEKOVA U BOSNI I HERCEGOVINI

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UVOD I CILJ

Bosna i Hercegovina je u 2017. godini prvi put implementirala podzakonski akt kojim se regulišu maksimalne veleprodajne cijene lijekova. Cilj rada bio je utvrditi uticaj regulisanih maksimalnih veleprodajnih cijena lijekova na tržište lijekova u Bosni i Hercegovini.

MATERIJAL I METODE

Izvršeno je poređnje cijena lijekova na tržištu u 2016. godini, kada cijene nisu bile regulisane, sa podacima o cijenama lijekova u 2017. godini kad je implementiran pravilnik po prvi put i sa podacima o cijenama lijekova u prvoj polovini 2018. godine. Izvori veleprodajnih cijena lijekova su bili podaci uvoznika i domaćih proizvođača u Bosni i Hercegovini za godišnje izvještaje o potrošnji lijekova koje naša agencija svake godine objavljuje na svojoj internet stranici www.almbih.gov.ba.

REZULTATI

Ukupna sredstva izdvojena za lijekove u 2017, i 2018. godini, niža su u odnosu na 2016. godinu na nivou iskazanog broja prometovanih pakovanja u 2016. godini. Veleprodajne cijene lijekova koji se izdaju na ljekarski recept u 2017. i 2018. godini niže su u odnosu na 2016. godinu. S druge strane, može se vidjeti da su veleprodajne cijene lijekova koji se izdaju bez ljekarskog recepta više u 2017., odnosno 2018. godini u odnosu na 2016. godinu. Bezreceptni lijekovi čine 15 % tržišta lijekova u Bosni i Hercegovini, tako da navedeno nije imalo velik uticaj na ukupna finansijska sredstva koja su izdvojena za lijekove u 2017., odnosno 2018. godini.

ZAKLJUČAK

Implementacija Pravilnika i uvođenje sistema maksimalnih veleprodajnih cijana lijekova ima pozitivan uticaj na tržište lijekova i na budžete fondova zdravstvenog osiguranja u Bosni i Hercegovini.

KJUČNE RIJEČI: maksimalne veleprodajne cijene lijekova

IMPACT OF THE RULEBOOK FOR REGULATION OF MAXIMAL WHOLESALE PRICES ON MEDICINE MARKET IN BOSNIA AND HERZEGOVINA

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INTRODUCTION

Bosnia and Herzegovina have implemented rulebook for regulating maximum wholesale prices at the first time in 2017. The aim of this study was to assess results of the influence of the rulebook on the level of wholesale prices of medicines on the market of Bosnia and Herzegovina.

METHODOLOGY

It was compared the level of wholesale prices in 2016 when rulebook has not existed with wholesale prices of medicines in 2017 when rolebook was implemented for the first time and with the data in first part of 2018. year. The wholesale prices of medicines were data obtaind from importers and domestic manufacturers which we collect every year for Annual reports about the distribution of medicines in Bosnia and Herzegovina and which are published on website www.almbih.gov.ba by our Agency.

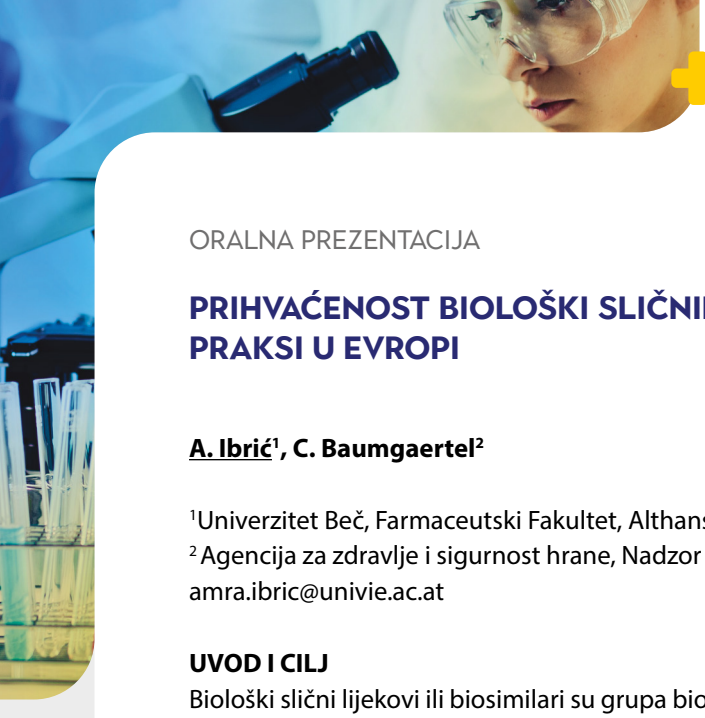
RESULTS

The total financial expenses for medicines was reduced in 2017, and in 2018. compared to 2016. Also, it was shown that the wholesale prices of Rx medicines in 2017. and 2018. are decreased compared with 2016. On the other side, it could be seen that OTC medicines have increased prices in 2017, respectively in 2018, as compared with the 2016 year. But, OTC medicines make 15% of the whole market of medicines and this increase did not have the influence on financial cost in all in 2017, respectively in 2018.

CONCLUSION

Implementation of the Rulebook and system of maximal wholsale prices of Rx medicines has positive influence on the market and budget of fonds for healthcare insurance in Bosnia and Herzegovina.

KEY WORDS: maximum wholesale prices of drugs



ORALNA PREZENTACIJA

PRIHVAĆENOST BIOLOŠKI SLIČNIH LIJEKOVA (BIOSIMILARA) U KLINIČKOJ PRAKSI U EVROPI

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UVOD I CILJ

Biološki slični lijekovi ili biosimilari su grupa bioloških lijekova koji su u pogledu kvalitete, efikasnosti i sigurnosti slični referentnom lijeku biološkog porijekla. S obzirom na visoke troškove liječenja biološkim inovativnim lijekovima, biosimilari su se pokazali kao izvrsna alternativa, budući da donose značajne uštede i omogućavaju pristup terapiji većem broju pacijenata. U etabliranju tržišta biosimilara posebno značajnu ulogu imaju zdravstveni radnici, od čije spremnosti da propisuju ove lijekove i savjetuju i prate pacijente zavisi i integracija biosimilara u svakodnevnu medicinsku praksu. U okviru master teze [1] sprovedena je elektronska studija među austrijskim ljekarima s ciljem proučavanja prihvaćenosti biosimilara. Rad također obuhvata i osvrt na slične studije sprovedene u drugim evropskim zemljama kao i opšte i zakonske odredbe te registraciju biosimilara na nivou Evropske Unije.

METODE

Elektronska anketa sprovedena je među austrijskim specijalistima iz oblasti reumatologije, gastroenterologije, onkologije i dermatologije, kao i među ljekarima opšte prakse koristeći online platformu SoSci Survey [2]. Kontakt i poziv na učešće je ostvaren pisanim putem. Za statističku obradu podataka korišteni su programi SPSS 25 i Microsoft Excel 2016.

Pregled dostupne literature izvršen je koristeći elektronske baze podataka poput PubMed i SciFinder. Studije sprovedene u Evropskoj Uniji, pisane na engleskom ili njemačkom jeziku bile su razmotrene.

REZULTATI

Iako svjesni prednosti i spremni da propisuju biosimilare, austrijski ljekari iskazali su određenu nesigurnost u primjeni biosmilara te smatraju da ljekari jos uvijek ne raspolažu sa dovoljno informacija o ovoj temi.

Slične studije u drugim evropskim zemljama otkrile su nedoumice među ljekarima u pogledu sigurnosti i efikasnosti biosimilara kao i zadršku pri njihovom propisivanju. Evidentni su i određeni nedostaci u znanju o biosimilarima.

ZAKLJUČCI

Studija među austrijskim ljekarima otkrila je djelimicno konzervativan pristup biosimilarima u ljekarskoj praksi, kao i potrebu boljeg informisanja.

Ostale evropske studije također su potvdile potrebu za poboljšanjem statusa biosimilara u svakodnevnoj medicinskoj praksi.

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KLJUČNE RIJEČI

biosmilari, anketa, zdravstveni radnici, klinička praksa

PHYSICIAN SURVEYS IN EUROPE: PERCEPTION OF BIOSIMILARS IN CLINICAL PRACTICE

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INTRODUCTION AND OBJECTIVE

Biosimilars are biologic therapeutic agents that are similar to an already licensed reference product in terms of quality, efficacy and safety. Due to the high costs of biologic therapies, biosimilars are seen as a viable alternative to expensive innovator biologics. Healthcare professionals play important role in establishing of biosimilar market and uptake of biosimilars depends greatly on their readiness to prescribe this medicines and inform the patient. As a part of master thesis [1] an online-based survey among Austrian physicians was conducted to analyse their additude toward biosimilars. Furthermore, the work comprises a review of published studies dealing with perception of biosimilars among European physicians, as well as general information about legal frames and registration of biosimilars in European Union.

METHOD

Online-based survey among Austrian physicians was conducted using online survey plattform SoSci Survey [2]. Specialty physician (total rheumatologists, gastroenterologists, oncologists and dermatologists countrywide) and a sample of general practitioners were contacted by letter and invited to take part in the survey. Statistical evaluation of data was conducted using SPSS 25 and Microsoft Excel 2016 software.

A literature research was conducted using electronic databases such as PubMed and SciFinder. Studies in English and German, conducted in European countries, were included.

RESULTS

Although willing to prescribe, Austrian physicians seem not to be completely comfortable with biosimilar term, complaining some lack of information.

European surveys in general expressed some efficacy and safety concerns as well as prescribing uncertainties, revealing also some gaps in biosimilar knowledge.

CONCLUSIONS

Austrian physicians survey highlighted some cautious approach towards biosimilars, indicating need for more information and better educational supply.

Surveys conducted among European physicians revealed current attitudes of healthcare providers toward biosimilars, leaving place for optimisation.

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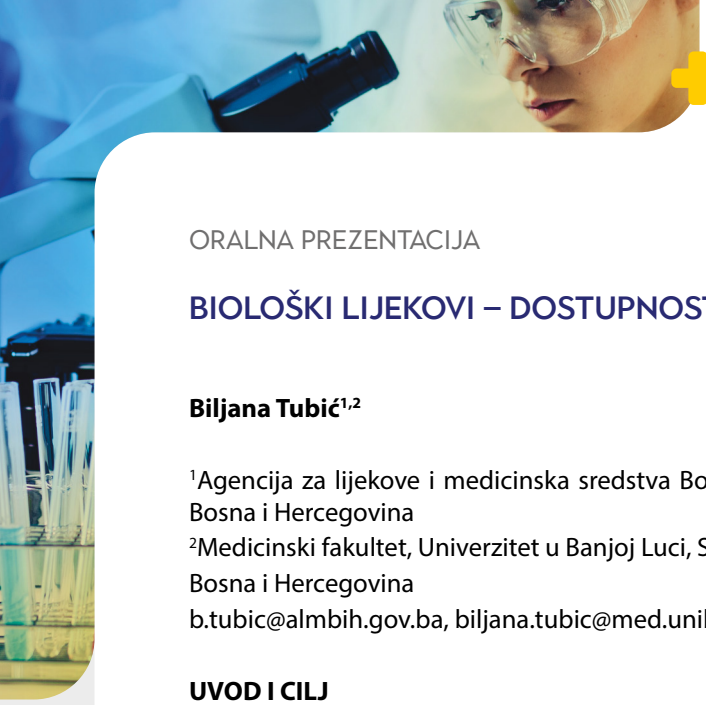
KEY WORDS

biosimilar, clinical practice, survey, physician



ORALNA PREZENTACIJA

BIOLOŠKI LIJEKOVI – DOSTUPNOST I REGULATIVA U BOSNI I HERCEGOVINI

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UVOD I CILJ

Primjenom bioloških lijekova postignuti su iskoraci u liječenju hroničnih oboljenja. Istekom perioda ekskluzivnosti podataka na tržište dospjevaju "kopije" referentnih bioloških lijekova (RBL) koje nazivamo slični biološki lijekovi ili biosimilari. Za razliku od proizvodnje sintetskih lijekova, proizvodnju bioloških lijekova iz živih organizama ne karakteriše visok stepen konzistentnosti. Navedeno uslovljava razlike u regulatornom pristupu pa se sličnost između RBL i biosimilara ocjenjuje po principu *„head–to–head"; „step-by-step"*, ali i široke stručne i naučne polemike po pitanju zamjenjivosti RBL sa biosimilarom tokom terapije. [1] U radu su prikazani regulatorni izazovi u odobravanju biosimilara u Bosni i Hercegovini (BiH), pregled registrovanih RBL i biosimilara, i ocjena njihove dostupnost u sistemu zdravstvene zaštite.

METODE

Korišteni su javno dostupni podaci Agencije za lijekove i medicinska sredstva BiH (ALMBIH), kao nadležne državne institucije za odobravanje lijekova.

REZULTATI

Za odobravanje biosimilara u BiH zahtjevaju se rezultati komparativnih studija, kojima se pokazuju sličnosti i razlike između biosimilara i RBL, a ocjenu istih radi ALMBIH primjenom smjernica Evropske agencija za lijekove. [2] Nije neophodno da biosimilar bude odobren za tržište EU prilikom prijave za registraciju u našoj zemlji.[2] Ukupno je za tržište BiH odobreno 238 bioloških lijekova (86 % RBL i 14 % biosimilara) što predstavlja 5,2 % svih registrovanih lijekova. Svi novoodobreni RBL i biosimilari su pod posebnim praćenjem.[2]

ZAKLJUČCI

Uprkos navedenom, visoka cijena i ograničene finansijske mogućnosti fondova zdravstvenih osiguranja uslovljavaju nezadovoljavajuću i nejednaku dostupnost bioloških lijekova i njihovih biosimilara. Stigma kod zdravstvenih radnika oko bezbjednosnog aspekta zamjenjivosti RBL sa biosimilarom dodani je razlog. Potrebno je podizati svijest zdravstvenih radnika i time otvarati mogućnosti za bolju dostupnost bioloških lijekova u BiH.

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KLJUČNE RIJEČI: dostupnost bioloških lijekova, biosimilari i referentni biološki lijekovi, regulativa

BIOLOGICAL MEDICINES – AVAILIBILITY AND REGULATION IN BOSNIA AND HERZEGOVINA

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INTRODUCTION

The use of biological medicines has contributed the progress in the treatment of chronic diseases. At the end of the period of data exclusivity, "copies" of reference biological medicines (RBMs) which referred as biosimilars, are coming to market. Unlike the production of small chemical medicines, the production of biological medicines from living organisms is not characterized by a high degree of consistency. This causes to differences in the regulatory approach - the similarity between RBM and biosimilars is evaluated on a "head-to-head" and" step-by-step". Also, observed differences between RBM and biosimilars are cause broad expert and scientific controversy regarding their interchangeability during the therapy. [1] In this paper it is presented the regulatory challenges in approving biosimilars in Bosnia and Herzegovina (B&H), review of approved RBMs and biosimilars, and evaluating of their availability in the health care system.

METHODS

The publicly available data of the Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina (ALMBIH), as the competent state institution for drug authorization, was used.

RESULTS

The approval of biosimilars in B&H requires from the pharmaceutical industry the results of comparative studies showing the similarities and differences between biosimilars and RBMs. Evaluation of the application is performed by ALMBIH using the guidelines of the European Medicines Agency. [2] It is not necessary for biosimilar to be approved for the European Union (EU) market when applying for marketing authorisation in our country. [2] In total, 238 biological drugs (86% of RBMs and 14% of biosimilars) have been approved for the B&H market, representing 5.2% of all approved medicines. All newly approved RBMs and biosimilars are under special monitoring. [2]

CONCLUSIONS

However, the high prices and limited financial capacity of founds of healthcare insurance make the insufficient and unequal availability of RBM and their biosimilars. The stigma of the healthcare professionals regarding the safety aspect of interchangeability of RBMs with biosimilars is an added reason insufficient of availability of biosimilars. It is necessary to raise awareness of health care professionals and thus open up opportunities for better availability of biological medicines in B&H.

LITERATURE

[1] https://www.ema.europa.eu/en
[2] https://www.almbih.gov.ba

KEY WORDS: dostupnost bioloških lijekova, biosimilari i referentni biološki lijekovi, regulativa

ORALNA PREZENTACIJA

HISTORIJSKI PREGLED RAZVOJA FARMACEUTSKOG ZAKONODAVSTVA U BOSNI I HERCEGOVINI – OD OSMANSKOG ISTOKA DO MODERNOG ZAPADA

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UVOD I CILJ

Farmacija je visokoregulirana društvena i naučna oblast. Prvi zakon koji je razdvojio farmaciju (apotekarstvo) i medicinu je poznat pod imenom Salernski edikt donesen od strane rimskog vladara Fridriha II iz 1240. godine. [1] Farmaceutska legislativa u Bosni i Hercegovini (BiH) pratila je razvoj države i državnog uređenja. S obzirom na ove historijske momente, sa aspekta farmacije možemo posmatrati razvoj legislative kroz šest razdoblja; 1. Samostalna srednjovjekovna Bosna, 2. Osmanski period, 3. Austro-ugarski period, 4. Stara Jugoslavija, 5. Socijalistička Jugoslavija i 6. Moderna BiH. [2]

METODE

Prikupljeni podaci analizirani su pretraživanjem literature u relevantnim bazama podataka, pregledom arhivske građe u muzejima i zdravstvenim ustanovama, te pretraživanjem interneta i razgovorima sa farmaceutima.

REZULTATI

U radu je dat detaljan pregled ključnih zakona kroz periode od samostalne srednjovjekovne Bosne, preko osmanskog i austro-ugarskog perioda, Kraljevine SHS, socijalističe Jugoslavije pa do današnjih dana i moderne BiH.

ZAKLJUČCI

Zakonodavstvo u historiji farmacije počelo se razvijati još od Osmanskog perioda i kroz promjene društvenog uređenja se usložnjavalo i pooštravalo. U modernoj BiH zakoni se prilagođavaju legislativi Evropske Unije i postoji veliki prostor za unapređenje i preciziranje pojedinih oblasti koje se trebaju urediti, posebno uzmemo li u obzir činjenicu da Zakon o lijekovima nje mijanjan od 2008. godine kada je donese.

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KLJUČNE RIJEČI: farmacija, zakonodavstvo, historija farmacije, apotekarstvo

HISTORICAL DEVELOPMENT OF PHARMACEUTICAL LEGISLATION IN BOSNIA AND HERZEGOVINA – FROM OTTOMAN EAST TO MODERN WEST

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INTRODUCTION AND OBJECTIVE

Pharmacy is highly regulated societal and scientific area. The first law separating the professions of physician and apothecary is Edict of Salerno declared by Roman Emperor Frederick II in 1240.[1] Pharmaceutical legislation in Bosnia and Herzegovina (BiH) followed state development and administration over the time. Given these historical points, we can observe the development of legislation over six periods from the pharmacy point of view; 1. Independent Medieval Bosnia, 2. Ottoman period, 3. Austro-Hungarian period, 4. Old Yugoslavia, 5. Socialist Yugoslavia and 6. Modern BiH. [2]

METHODS

The data collected were analyzed by searching the literature in relevant databases, reviewing archives at museums and health institutions, and searching the Internet and interviewing pharmacists.

RESULTS

In this work a detailed overview of the key legislative acts is presented starting from Independent Medieval Bosnia, Ottoman period, Austro-Hungarian period, Old Yugoslavia, Socialist Yugoslavia and Modern BiH.

CONCLUSIONS

Legislation in the history of pharmacy began to develop from the Ottoman period, and through social changes changed and became more complex. In modern BiH, laws are aligned with European Union legislation, and there is ample room for improvement and refinement of certain areas that need to be regulated, especially considering the fact that the Medicines Law has been changing it since 2008.

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KEY WORDS: pharmacy, legislation, history of pharmacy, apothecary

ORALNA PREZENTACIJA

PREDSTAVLJANJE PRVOG, HRVATSKOG PRIRUČNIKA ZA SAMOLIJEČENJE

M. Radošević

Hrvatska udruga proizvođača bezreceptnih proizvoda (CASI)

Hrvatska udruga proizvođača bezreceptnih proizvoda (CASI) izdala je prvi i sveobuhvatni *Priručnik za samoliječenje* s ciljem podizanja kvalitete savjeta pacijentima današnjih i budućih ljekarnika. Priručnik opsegom i kvalitetom sadržaja predstavlja jedinstveno izdanje i izvan granica Hrvatske, a rezultat je suradnje velike skupine ljekarnika s iznimnim iskustvom svakodnevnoga rada s pacijentima, predstavnika farmaceutske industrije, liječnika obiteljske medicine te Hrvatske agencije za lijekove i medicinske proizvode, Hrvatskoga zavoda za javno zdravstvo, Farmaceutsko-biokemijskoga fakulteta Sveučilišta u Zagrebu i Hrvatske ljekarničke komore. Priručnik detaljno opisuje najčešće manje zdravstvene tegobe s kojima se ljekarnici svakodnevno susreću u radu s pacijentima, s konkretnim savjetima kako mogu pomoći građanima i kvalitetno ih savjetovati. Priručnik je alat za sve ljekarnike koje potiče na savjetovanje pacijenata o minornim bolestima na znanstveno utemeljen način, što kao krajnji cilj ima i rasterećenje javnozdravstvenog sustava Hrvatske. Priručnik je također pripremljen i u *on-line* verziji kako bi kontinuirano mogao biti dostupan ljekarnicima. *On-line* izdanje izrađeno je u *web* sučelju prilagođenom za korisničku uporabu. *Web* sučelje omogućava jednostavno čitanje i pretraživanje sadržaja uz kvalitetan korisnički doživljaj.

Nakon ovog predavanja sudionici će usvojiti:

- Važnost ljekarnika u sustavu odgovornog samoliječenja
- Pozitivan utjecaj odgovornog samoliječenja na javnozdravstveni sustav Hrvatske
- Značaj priručnika za samoliječenje u promociji odgovornog samoliječenja na znanstveno utemeljen način
- Jednostavnost korištenja on-line izdanja Priručnika za samoliječenje

SOCIJALNA FARMACIJA I ZAKONODAVSTVO

SOCIAL PHARMACY AND LEGISLATION

POSTER

FARMAKOEKONOMSKA ANALIZA POTROŠNJE ANTIDIJABETIKA U KANTONU SARAJEVO

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UVOD I CILJEVI

Diabetes mellitus je naziv za grupu metaboličkih bolesti kojima je zajednički simptom hiperglikemija. U Bosni i Hercegovini (BiH) problem predstavlja nepostojanje jedinstvenog registra oboljelih. Prema podacima Federalnog zavoda za statistiku, prevalencija dijabetesa u Federaciji BiH je 54,8/100 000 stanovnika. Bolest, kao i njene komplikacije, predstavljaju ekonomsko opterećenje za pacijente, porodicu, a i društvo u cijelosti. Najbolji lijek je kvalitetan, djelotvoran i siguran, ali i ujedno cjenovno najpovoljniji. Farmakoekonomskim analizama cilj je izbalansirati trošak i ishod liječenja te ponuditi najoptimalnije rješenje za terapiju. Cilj rada je da se prikaže potrošnja antidijabetika u Kantonu Sarajevo i da se izvede analiza minimizacije troškova (CMA – eng. *Cost minimisation analysis*) za najčešće propisivane oralne antidijabetike, metformin i glimepirid.

METODE

U radu su obrađeni podaci za 63 antidijabetika, koji se nalaze na A ili B listi lijekova Zavoda zdravstvenog osiguranja Kantona Sarajevo (ZZOKS). Podaci o potrošnji antidijabetika na području Kantona Sarajevo dobiveni su od strane ZZOKS. Analiza je obuhvatila 2016. godinu. Za CMA su uzeti u obzir samo direktni troškovi.

REZULTATI

Najčešće propisivani antidijabetici iz grupe inzulina su bili inzulini i analozi srednje dugog djelovanja u kombinaciji sa inzulinima brzog djelovanja (ATC A10AD), sa učešćem od 50,90% od ukupnog broja propisivanih inzulina. Iz grupe oralnih antidijabetika najčešće propisivani je bio metformin (ATC A10BA02) sa učešćem od 61,79% od ukupnog broja propisivanih oralnih antidijabetika. CMA analizom utvrđeno je da su troškovi za liječenje jednog pacijenta metforminom, na godišnjem nivou, 87,60 KM, što je za 1,90 puta više u odnosu na terapiju glimepiridom, gdje su troškovi 46,23 KM.

ZAKLJUČCI

Od ukupnih sredstava izdvojenih od strane ZZOKS za lijekove u 2016. godini, 23% čine troškovi terapije dijabetesa, što je oko 18 miliona KM. Najbitnije je raditi na prevenciji pojave dijabetesa, ali istovremeno se treba posvetiti boljem farmakoekonomskom planiranju u cilju racionalizacije potrošnje antidijabetika.

KLJUČNE RIJEČI: dijabetes, farmakoekonomska analiza

PHARMACOECONOMIC ANALYSIS OF THE CONSUMPTION OF ANTIDIABETICS IN SARAJEVO CANTON

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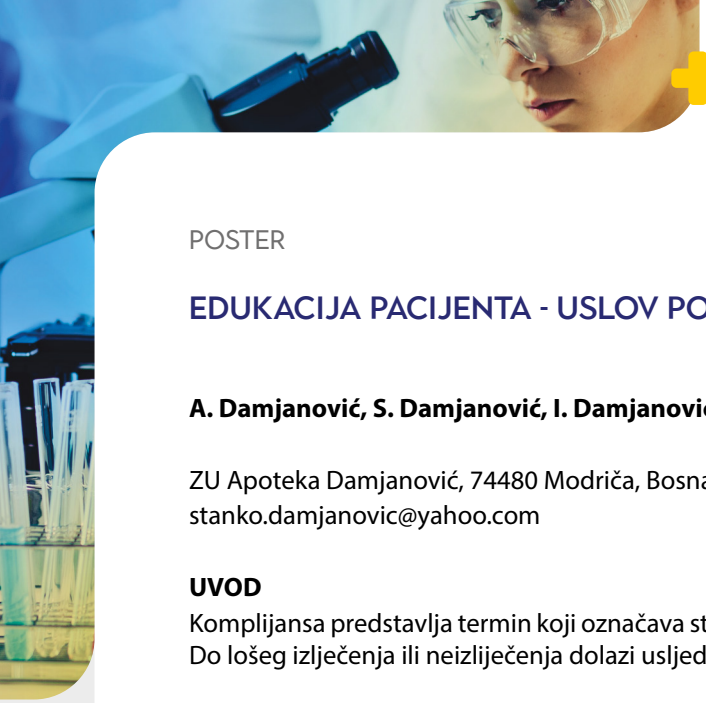
INTRODUCTION AND OBJECTIVE
Diabetes mellitus is the name for a group of metabolic diseases with common symptom of hyperglicemia. Main problem in Bosnia nad Herzegovina is lack of unique registry of patients. According to the Federal Office of Statistics, the prevalence of diabetes in the Federation of Bosnia nad Herzegovina is 54,8/100 000. Disease, as well as its complications, are an economic burden for patients, the family, and whole society. The best drug is quality, effective and safe, but in the same time, one with the best price. Aim of pharmacoeconomic analysis is to balance the cost and outcome of treatment and to offer the most optimal treatment solution. The aim of the paper is to show the consumption of antidiabetic drugs in Sarajevo Canton and to perform the Cost minimization analysis (CMA) for commonly prescribed oral antidiabetic drugs, metformin and glimepiride.

METHODS
The paper analyzes the data for 63 antidiabetics, which are on the A or B list of medicines of the Health Insurance Institute of Sarajevo Canton (HIISC). Data on the consumption of antidiabetic drugs in Sarajevo Canton were obtained from the HIISC. The analysis covered 2016 year. Only direct costs were considered for the CMA.

RESULTS
The most commonly prescribed antidiabetics in the insulin group were insulin and medium-acting analogues in combination with fast-acting insulin (ATC A10AD), with a proportion of 50,90% of the total number of prescribed insulins. The most commonly prescribed oral antidiabetic was metformin (ATC A10BA02) with a proportion of 61,79% of the total number of oral antidiabetic drugs prescribed. CMA showed that the cost of treating one patient with metformin was 87,60 KM annually, which was 1,90 times higher than glimepiride therapy, where the costs were 46,23 KM.

CONCLUSIONS
Of the total funds allocated by the HIISC in 2016, 23% was for costs of diabetes therapy, which is approximately 18 million KM. It is essential to work on prevention of diabetes, but at the same time, should be devoted to better pharmacoeconomic planning with aim of rationalizing antidiabetic consumption.

KEY WORDS: diabetes mellitus, pharmacoeconomic analysis



POSTER

EDUKACIJA PACIJENTA - USLOV POVEĆANJA STEPENA KOMPLIJANSE

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UVOD

Komplijansa predstavlja termin koji označava stepen koliko bolesnik slijedi uputstva ljekara u primjeni lijekova. Do lošeg izlječenja ili neizliječenja dolazi usljed niskog stepena komplijanse [1].

CILJ

Dobra Apotekarska Praksa je sistem osiguranja kvaliteta usluga koje pacijent dobija u apoteci. Jedan od osnovnih ciljeva Dobre Apotekarske Prakse je briga farmaceuta za bolesnikovo zdravlje, te je u tom kontekstu uloga farmaceuta u edukaciji pacijenta veoma značajna [2]. Kombinacija znanja, vještine i brige za bolesnikovo zdravlje, obezbijedili su farmaceutu mjesto zdravstvenog stručnjaka odgovornog za prevenciju bolesti, promociju zdravlja i sprovođenje bezbijedne, efikasne i ekonomične farmakoterapije. Pacijenta je potrebno edukovati kako bi u potpunosti shvatio značaj redovne prepisane mu terapije kao i posljedice nepoštovanja propisanih uputstava. Edukovan pacijent želi da aktivno učestvuje u kontroli svojih zdravstvenih problema čime sam povećava stepen komplijanse [3]. Farmaceut, kao član zdravstvenog tima, mora poznavati moguće razloge niskog stepena komplijanse, kako bi aktivno uticao na umanjenje ili otklanjanje prepoznatih razloga. Treba da edukuje pacijenta o značaju redovne terapije, posljedicama nepoštovanja propisanih uputstava te da izgradi dobar odnos sa pacijentom u smislu razumijevanja, pristupačnosti, komunikativnosti i pozitivnog stava, što predstavlja imperativ za podršku komplijsnsi.

ZAKLJUČAK

Uspostavom pozitivne komunikacije preko lijeka sa pacijentom te stvaranjem osjećaja bliskosti, povjerenja i brige za njegovo zdravlje, farmaceut će trajno ostati dobar prijatelj i stručni savjetnik svojim pacijentima.

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KLJUČNE RIJEČI: Dobra Apotekarska Praksa, edukacija, komplijansa

EDUCATION OF PATIENTS - CONDITION FOR INCREASING THE LEVEL OF COMPLIANCE

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INTRODUCTION

Compliance is a term that stands for the level of how much a patient follows the doctor's instructions in the use of medications. The low level of the compliance leads to the poor healing or non-healing [1].

OBJECTIVE

A Good Pharmaceutics Practice is a system of providing the quality of services that a patient gets at a pharmacy. One of the basic goals of a Good Pharmaceutics Practice is a pharmacist's care for the patient's health, therefore the role of the pharmacist in the education of patients is very significant [2]. The combination of knowledge, skills and care for the patient's health has provided a pharmacist the role of a health expert responsible for prevention of diseases, promotion of health and running a safe, efficient and economical pharmacotherapy. A patient needs to be educated in order to realise the importance of the regular prescribed therapy, as well as the consequences of not following the prescribed instructions. An educated patient wants to take an active part in controlling their health problems, by which they increase the level of compliance themselves [3]. A pharmacist, as a member of the medical team, has to know the possible reasons for the low level of compliance, in order to actively influence the decreasing or elimination of those recognised. They need to educate the patient on the importance of the regular therapy, the consequences of not following the prescribed instructions, as well as to build a good relationship with the patient, in the sense of understanding, accessibility, communication skills and a positive attitude, which is an imperative for supporting the compliance.

CONCLUSION

By establishing a positive communication with a patient, through a medication, and creating the feeling of closeness, trust and care for their health, a pharmacist will permanently remain a good friend and an expert advisor to their patients.

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KEYWORDS: Good Pharmaceutics Practice, education, compliance

POSTER

MIŠLJENJA I STAVOVI STUDENATA FARMACIJE O PROGRAMU STRUČNOG OSPOSOBLJAVANJA

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UVOD I CILJ

Od akademske godine 2011./2012., Farmaceutsko-biokemijski fakultet Sveučilišta u Zagrebu (FBF) provodi šestomjesečni program stručnog osposobljavanja studenata farmacije (SOF) temeljen na Hrvatskom ljekarničkom kompetencijskom okviru (HLJKO) [1]. Cilj ovog istraživanja bio je prikazati mišljenja i stavove studenata farmacije o novom programu SOF-a.

METODE

U studiju su uključeni studenti FBF-a koji su u ak. god. 2015./2016. i 2016./2017. sudjelovali na SOF-u. Podaci su prikupljeni kroz dva anonimna anketna upitnika za studente (jedan o program SOF-a i drugi o mentoru u javnoj ljekarni). Svaki upitnik sastojao se od kvantitativnog (prikazan u ovom istraživanju) i kvalitativnog dijela. Studenti su mogli izraziti stavove i stupanj zadovoljstva na skali 1-5, pri čemu je 1 najniži, a 5 najviši stupanj slaganja s pojedinom tvrdnjom. Ankete su upućene studentima po završetku SOF-a putem sustava za e-učenje Merlin, uz zajamčenu anonimnost pri ispunjavanju obaju upitnika.

REZULTATI

Ukupno je 126 studenata sudjelovalo u istraživanju. Većinu su činile osobe ženskog spola (87,3%). Najveći udio studenata (47,6%) izrazio je srednji stupanj zadovoljstva programom SOF-a (ocjena 3 na skali 1-5), dok ih je 3,8% bilo u potpunosti zadovoljno. Najveći udio studenata iskazao je najveće zadovoljstvo mentorom u javnoj ljekarni (61,7%). Studentska mišljenja o važnosti samoprocjene prema HLJKO-u su podijeljena, a samo manji broj to smatra iznimno bitnim (15,3%). Preko 60% studenata smatra da su im za rad u ljekarni nepotpuna znanja iz područja bezreceptnih lijekova, dermatofarmacije te dodataka prehrani i prve pomoći. Većina (93,7%) iskazala je visoko zadovoljstvo odnosom mentora prema studentu, dok je najniže ocijenjena potpora mentora pri izradi portfolia za SOF.

ZAKLJUČCI

Istraživanje je pokazalo da su prve generacije studenata prema novom programu SOF-a iznimno zadovoljne mentorima-ljekarnicima koji ih vode kroz SOF. Identificirana su također područja u okviru SOF-a, ali i samog studija farmacije FBF-a, koja treba dodatno razvijati s ciljem poboljšanja kvalitete studija te unapređenja studentskih kompetencija.

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KLJUČNE RIJEČI: stručno osposobljavanje, studij farmacije, mentori, javna ljekarna, kompetencije

OPINIONS AND ATTITUDES OF PHARMACY STUDENTS TOWARDS THE PROFESSIONAL TRAINING PROGRAM

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INTRODUCTION AND OBJECTIVE

Since the academic year 2011/2012, the Faculty of Pharmacy and Biochemistry, University of Zagreb (FBF), has been implementing a six-month professional training program for pharmacy students (SOF) based on the Croatian Competency Framework for Pharmacists (GbCF) [1]. The aim of this research was to present the opinions and attitudes of pharmacy students about the new SOF program.

METHODS

This study includes FBF students who participated in SOF program during the academic years 2015/2016 and 2016/2017. The data were collected through two different anonymous student's questionnaires (one about the SOF program and another about the pharmacy mentor). Each questionnaire consisted of a quantitative (presented in this research) and a qualitative section. Students were able to express attitudes and satisfaction on a scale from 1 to 5, with 1 being the lowest and 5 being the highest level of agreement with each statement. Upon completion of the SOF program, questionnaires were sent to students via Merlin e-learning system, with guaranteed anonymity when completing both questionnaires.

RESULTS

A total of 126 students participated in the survey. The majority was female (87.3%). The highest proportion of students (47.6%) expressed a medium degree of satisfaction with the SOF program (grade 3 on a scale 1-5), while 3.8% were completely satisfied. The highest proportion of students reported the highest satisfaction with a mentor in a community pharmacy (61.7%). Students' opinions are divided about the importance of self-assessment according to the GbCF and only a small number of students consider it extremely important (15.3%). Over 60% of students believe they lack knowledge needed for work in the pharmacy in the fields of over-the-counter medications, dermatopharmacy, dietary supplements and first aid. The majority (93.7%) of students expressed high satisfaction with the mentor-student relationship, while the lowest rate was given to mentor's support in writing the portfolio for SOF.

CONCLUSIONS

The research showed that the first generations of students are extremely satisfied with the pharmacists' mentors who guide them through the SOF under the new SOF program. In addition, it has been identified need for further development of areas within the SOF, as well as the FBF pharmacy study program itself, in order to improve the quality of studies, as well as to improve students' competencies.

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KEY WORDS: professional training, pharmacy studies, mentors, public pharmacy, competencies

POSTER

DOSTUPNOST PRIMARNE PREVENCIJE STUDENTSKOJ POPULACIJI

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UVOD I CILJ

Početak studiranja poklapa se sa prelaskom mladih osoba iz adolescencije u odraslo doba, pa oni često i eksperimentišu sa novim životnim stilovima [1]. Tokom ovog perioda života, studenti su skloniji da se uključe u rizična zdravstvena ponašanja, kao što su fizička neaktivnost, stres, loše navike u ishrani, konzumiranje duvanskih proizvoda, alkohola i psihoaktivnih supstanci [2]. Cilj ove studije bio je da se ispitaju stavovi studenata u vezi sa dostupnošću primarne prevencije u studentskim domovima.

METODE

Sprovedena je prospektivna studija po dizajnu studije preseka, uz odgovarajući upitnik u studentskoj populaciji koja tokom studiranja stanuje u studentskim domovima. Studenti koji su učestvovali u istraživanju su stanovnici 10 studentskih domova Studentskog Centra Beograd. Prikladan uzorak je definisan kao 10% ukupnog broja studenata po svakom domu. Istraživanje je sprovedeno od aprila do septembra 2018. godine.

REZULTATI

Ukupan broj ispitanika bio je 996. U istraživanju je učestvovao nešto veći procenat muškaraca nego žena (51.1% vs 48.9%). Najveći broj ispitanika odgovorio je da odlazi kod lekara opšte prakse samo kada imaju neki zdravstveni problem (64.8%). Razlog za ovako slab odlazak kod lekara po stavovima ispitanika je taj što nemaju naviku preventivnog odlaska kod lekara. Od ukupnog broja ispitanika, 86.5% smatra da je potrebno da u okviru studentskog doma postoji zdravstvena ambulanta. Najznačijna zdravstvena služba u studentskoj ambulanti, po stavovima studenata je postojanje lekara opšte prakse (82.3%), dok 68.6% ispitanika smatra da je potrebno da se u okviru studentskog doma nalazi i apoteka.

ZAKLJUČCI

Za primarnu prevenciju značajni su preventivni pregledi studenata, ali i edukacija i stvaranje pozitivnog stava kod studenata o značaju primarne prevencije i zdravim stilovima života.

Dostupnost primarne prevencije potrebno je poboljšati, kroz zdravstvene servise i edukacije koje mogu poboljšati dostupnost zdravstvene zaštite studentima.

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KLJUČNE RIJEČI: studenti, primarna prevencija, životni stilovi

Zahvalnica: *Rad je urađen u okviru projekata 175036 i 41004 koje finansira Ministarstvo prosvete, nauke i tehnološkog razvoja Republike Srbije.*

AVAILABILITY OF PRIMARY PREVENTION TO THE STUDENT POPULATION

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INTRODUCTION AND OBJECTIVE

The beginning of college studies coincides with the transition from adolescence to adulthood, hence young students often experiment with new lifestyles [1]. During this period of life, students are more prone to engage in risky health behaviors, such as physical inactivity, stress, unhealthy diet, tobacco and alcohol consumption, and psychoactive substances abuse [2]. The aim of this study was to examine student attitudes in relation to the availability of primary prevention in dormitories.

METHODS

A prospective cross-sectional study was conducted using an appropriate questionnaire among the student population residing in the dormitories during their studies. The students who participated in the survey were residents of 10 dormitories of the Student Center Belgrade. An adequate sample was defined as 10% of the total number of students per each dormitory. The survey was conducted from April to September 2018.

RESULTS

The total number of respondents was 996. A slightly larger percentage of men than women participated in the survey (51.1% vs 48.9%). The majority of respondents visited a general practitioner only when facing a health problem (64.8%). Such poor record of visiting physicians, according to the attitudes of the respondents, was due to unestablished habit of preventive screening. 86.5% of the respondents believed that there was a need for having a health clinic within dormitories. The most significant health service required, according to the students, was that of general practitioners (82.3%), while 68.6% of respondents believed that it was necessary to have a pharmacy within dormitories as well.

CONCLUSIONS

Preventive examinations of students are important for primary prevention, as well as education and influencing positive attitude among students toward the importance of primary prevention and healthy lifestyles. The availability of primary prevention needs to be improved, through healthcare services and education that can lead to broader healthcare available to students.

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KEY WORDS: students, primary prevention, lifestyles

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POSTER

FARMAKOTERAPIJSKA PISMENOST (PTHL) RODITELJA PREDŠKOLSKE DECE U RURALNOJ I URBANOJ SREDINI U SRBIJI

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UVOD I CILJEVI

Farmakoterapijska pismenost (PTHL) predstavlja sposobnost pojedinca da pronađe, proceni, izračuna i razume osnovne informacije o farmakoterapiji i uslugama apoteke koje su neophodne za donošenje odgovarajućih odluka koje se odnose na lekove [1]. Cilj studije je bilo određivanje nivoa farmakoterapijske pismenosti kod roditelja predškolske dece (do 7 godina) u ruralnoj i urbanoj sredini u Srbiji i ispitivanje socio-demografskih karakteristika i zdravstvenih navika koje imaju uticaja na farmakoterapijsku pismenost.

METODE

Sprovedena je studija preseka među roditeljima predškolske dece u vrtićima opštine Koceljeva (ruralna sredina) i u vrtićima Novog Beograda (urbana sredina) od maja do juna 2019. godine. Validirani instrument za samoprocenu farmakoterapijske pismenosti roditelja na srpskom jeziku (*Parental pharmacotherapy literacy questionnaire—Serbian*), je korišćen da bi se ispitalo znanje, razumevanje i numeričke veštine neophodne za bezbednu upotrebu lekova. Prema nivoima, roditelji su podeljeni u grupe sa niskom, srednjom i visokom PTHL. Socio-demografske karakteristike i zdravstvene navike su takođe ispitane. Korišćena je deskriptivna statistika i parametarski testovi sa verovatnoćom $p<0.05$ kao značajnom.

REZULTATI

Ispitano je ukupno 432 roditelja (250 iz urbane i 182 iz ruralne sredine). Najviši rezultat PTHL je postiglo 11.7% žena i 2.7% muškaraca u ruralnoj populaciji, a u urbanoj 27.1% žena i 23.3% muškaraca. U urbanoj sredini, viši rezultati PTHL su bili povezani sa nivoom obrazovanja ($p< 0.001$), roditeljima sa više dece ($p< 0.001$) i starijim roditeljima ($p< 0.05$). U ruralnoj sredini, nivo obrazovanja nije imao uticaj na PTHL, ali starost roditelja jeste. Najmlađi roditelji iz ruralne sredine su pokazali najniži nivo PTHL (68,9%, $p<0,05$), dok su stariji roditelji uglavnom pokazali srednji nivo farmakoterapijske pismenosti (41,5%, $p<0,05$).

ZAKLJUČAK

Studijom je pokazano da roditelji predškolske dece u ruralnoj sredini u Srbiji imaju niži nivo PTHL nego roditelji iz urbane sredine. Potrebno je kreirati efektivne programe za prevenciju i upravljanje niskim nivoom PTHL, kroz promociju bolje dostupnosti informacija o lekovima u ruralnoj sredini.

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KLJUČNE REČI: farmakoterapijska pismenost, roditelji, predškolska deca, ruralna sredina, bezbednost

Zahvalnica: *Rad DK je u okviru projekta Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije, br. Projekta 41004.*

PHARMACOTHERAPY LITERACY (PTHL) OF PARENTS OF PRE-SCHOOL CHILDREN IN RURAL VS. URBAN AREA OF SERBIA

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INTRODUCTION AND AIM

Pharmacotherapy literacy (PTHL) is an individual's capacity to obtain, evaluate, calculate, and comprehend basic information about pharmacotherapy and pharmacy related services necessary to make appropriate medication-related decisions [1]. We aimed to determine PTHL levels among parents of pre-school children (up to 7 years old) in rural and urban area of Serbia and to analyze socio-demographic and health related characteristics related to levels of pharmacotherapy literacy.

METHODS

Conducted study was cross-sectional, with parents of pre-school children in kindergartens in the Municipality of Koceljeva (rural area), and Novi Beograd (urban area). From May to June 2019, validated, self-percepted instrument (Parental pharmacotherapy literacy questionnaire— Serbian) was used to assess knowledge, understanding and numerical skills necessary for safe use of medicines. According to PTHL levels, parents were classified in groups with low, medium and high PTHL. Socio-demografic and health-related characteristics were also collected. Descriptive statistics and parametric tests were used with $p< 0.05$ set as significant.

RESULTS

Overall, 432 parents were surveyed (250 from urban, and 182 from rural area). The highest results of PTHL were achieved by 11.7% females and 2.7% males from rural population, while in urban, by 27.1% females and 23.3% males. In urban population, higher PTHL was correlated with education ($p < 0.001$), parents with more children ($p < 0.001$) and older parents ($p < 0.05$). In rural populations, level of education didn't have any influence on PTHL results, but age had. The youngest parents from rural area were with lowest levels (68,9%, $p<0,05$), while older parents showed medium levels (41,5%, $p<0,05$) of PTHL.

CONCLUSIONS

Our study showed that parents of pre-school children in rural area of Serbia have lower levels of PTHL than parents from urban area. It is necessary to make effective programs for prevention and management of low PTHL, in promoting better access to medicines related information in rural populations.

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KEY WORDS: pharmacotherapy literacy, parents, pre-school children, rural area

Acknowledgment: *The work of DK is carried out under the Project funded by the Ministry of Education, Science and Technological Development of the Republic of Serbia, Grant Number 41004.*

POSTER

UVERENJA FARMACEUTA O POLITICI U VEZI SA ORFAN LEKOVIMA U SRBIJI

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UVOD I CILJ

Uprkos činjenici da se zahvaljujući evropskim i nacionalnim regulativama otvaraju nove perspektive u oblasti lečenja retkih bolesti (RB), do danas su dostupne terapije za samo 5% obolelih od retkih bolesti [1,2]. Cilj rada je da se analiziraju uverenja farmaceuta o politici orfan lekova (POL) i skrene pažnja istraživačima, kreatorima politike, zdravstvenim profesionalcima, pacijentima i farmaceutskim kompanijama na faktore koji mogu da optimizuju nacionalnu POL.

METODE

Studija preseka sprovedena je u javnim apotekama u Srbiji 2014. godine sa namenski kreiranim upitnikom. Prikupljene su socio-demografske karakteristike ispitanika. Putem petostepene Likertove skale procenjena su uverenja farmaceuta o 15 pitanja u vezi sa politikom orfan lekova.

REZULTATI

U istraživanju je učestvovalo ukupno 559 farmaceuta. Više od polovine ispitanika se u potpunosti slaže da: (i) svako ima pravo na jednak pristup zdravstvenoj zaštiti (70.9%); (ii) Oboleli od retkih bolesti treba da imaju prava na besplatno lečenje pojedinim lekovima iako je terapija veoma skupa (60.8%); (iii) retka bolest ugrožava ekonomsku situaciju porodice/staratelja obolelog (65.9%); (iv) nedostunost terapije je posledica siromaštva (56.6%); i toga što, zbog malog broja obolelih, lekovi nisu registrovani (67.3%).

Oko polovine ispitanika slaže se da je nemogućnost preduzimanja farmakoloških mera u lečenju posledica nepostojanja efikasnog leka (52.4%;); zdravstvene vlasti treba da koriste resurse za postizanje najvećih zdravstvenih beneficija (58.4%) i prepoznaju nedostatak javne svesti u društvu u vezi sa RD (46.4%).

Ne postoji statistički značajna razlika između muškaraca i žena po pitanju stavova i mišljenja u vezi sa lekovima i lečenjem i značaju koji ova pitanja imaju za javno zdravlje. Jedino se nešto veći procenat žena u većem stepenu slaže sa tvrdnjom da je „neadekvatno ulaganje u podsticaje za istraživanje i razvoj lekova za RD (x^2=10,87; $p<0,05$). Ne postoji statistički značajna razlika između ispitanika sa diplomskim i poslediplomskim nivoom obrazovanja po pitanju stavova i mišljenja u vezi sa RD. Dužina radnog staža u vezi je sa razlikama po pitanju sledeće tvrdnje: „svako ima pravo na jednak pristup zdravstvenoj zaštiti“ ($x^2=34,99$; p<0,01)

ZAKLJUČCI

Rezultati istraživanja ukazuju da farmaceuti u Srbiji prepoznaju potrebe obolelih od retkih bolesti i umeju da identifikuju ključne zdravstvene, društvene, ekonomske, pravne i etičke faktore koje treba da pruži zdravstveni sistem na nacionalnom nivou u cilju pružanja dostupne i pravične zdravstvene zaštite.

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KLJUČNE RIJEČI: retke bolesti, orfan lekovi, farmaceuti, stavovi, politika lekova

Zahvalnica: *This research was supported by the grant of Ministry of Education, Science and Technological Development in Serbia, Grant Number 41004.*

SERBIAN PHARMACISTS' ATTITUDES ON ORPHAN DRUG POLICY

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INTRODUCTION AND OBJECTIVE
Despite the fact that new perspectives are opening up in the area of rare diseases (RD) due to European and national regulations, it is estimated that treatments for only 5% of patients are available [1,2]. The aim of this study was to analyze pharmacists' attitudes on orphan drug policy (ODP) and draw attention to researchers, health policy creators, health professionals, patients and pharmaceutical companies on the factors that may optimize national orphan drug policy.

METHODS
The prospective cross-sectional study was conducted in the community pharmacies in Serbia. Socio-demographic characteristics of the respondents were collected, and pharmacists' attitudes on the ODP were evaluated through 15 items using a five-point Likert scale.

RESULTS
In total, 559 pharmacits participated. More than half of the respondents agree that: (i) everyone should have equal access to health care (70.9%); (ii) patients with RD should have the right to chouse treatment with some drugs even if the treatment itself is expensive (60.8%); (iii) RD impacts negatively the economic situation of the patients` family/ guardians (65.9%); (iv) poverty might be a cause of the lack of treatment and therapy (56.6%); and that, due to a limited number of patients, new orfan drugs were not registered (67,3%).
About half of the respondents agreed that a lack of appropriate pharmacologic measure in treatment was the consequence of the lack of an effective drug (52.4%;); health authorities should use resources to achieve the greatest health benefits (58.4%). Only 46.4% recognizeed the lack of public awareness regarding RD.
There is no statistically significant difference between men and women in terms of attitudes and opinions regarding treatment and the importance of these issues for public health. Only a slightly higher percentage of women more strongly agreed with the statement that "there are inadequate incentives for investment into research and development for RD" ($x2 = 10.87$; $p < 0.05$). There was no statistically significant difference between respondents with graduate and postgraduate levels of education in terms of attitudes and opinions regarding RD. The length of work experience is related to differences in attitudes in respect of equal availability of everyone to health care in rare diseases. ($x2 = 34.99$; $p < 0.01$).

CONCLUSIONS
Research findings indicate that pharmacists in Serbia understand the needs of patients with RD and are able to identify key health, social, economic, legal and ethical factors that healthcare system at the national level must provide foraccessible and equitable healthcare for RD patients.

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KEY WORDS: rare diseases, orphan drugs, pharmacists, attitudes, health policy

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POSTER

ŠIRENJE APOTEKARSKE MREŽE: TRAGOM OGLASA ZA OTVARANJE PETNAESTE BEOGRADSKE APOTEKE S POČETKA XX VEKA

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UVOD I CILJ

Privredni razvoj i povećanje broja stanovnika u Srbiji početkom prošlog veka uslovilo je potrebu za otvaranjem novih apoteka, posebno u velikim graodovima. Ministarstvo unutrašnjih poslova je prema Zakonu o sanitetskoj struci i o čuvanju narodnog zdravlja određivalo rejon i mesto za otvaranje apoteka. Cilj rada je da se prikaže uloga države u uspostavljanju mreže javnih apoteka kroz prikaz konkursa za otvaranje XV beogradske apoteke.

METODE

U radu je korišćena istorijska metoda i dokumentaciona analiza primarnih i sekundarnih izvora podataka.

REZULTATI

Početkom XX veka u Srbiji su na snazi bile dve vrste koncesija za otvaranje apoteka: a) na osnovu „realnog prava“, ukoliko sopstvenik apoteke nije stručno lice; i b) na osnovu „personalnog (ličnog) prava“ po kome je apoteku mogao otvoriti i držati isključivo magistar ili doktor farmacije srpske nacionalnosti sa dobrim vladanjem ili stranac koji će za godinu dana dobiti srpsko državljanstvo. Ministarstvo unutrašnjih dela uređivalo je mrežu apoteka u Srbiji kroz planiranu dodelu koncesija sa jasno utvrđenim rejonima i mestima za otvaranje apoteka. Dana 3. juna 1906. godine objavljen je konkurs za otvaranje petnaeste beogradske apoteke [1]. Od deset farmaceuta iz unutrašnjosti koji su želeli da premeste svoje apoteke u Beograd, pravo na otvaranje apoteke u rejonu »Savinac« dobio je farmaceut Velimir Karić, vlasnik apoteke u Vranju sa najviše godina apotekarske prakse [2]. Postupak dobijanja dozvole za apoteku u Beogradu pokrenulo je niz pitanja o pravu na dodelu nove koncesije farmaceutima koji su želeli da otuđe ili vrate postojeće. Ministarstvo unutrašnjih poslova je po pravu vrhovnog nadzora regulisalo pitanje rejona, mesta i prava farmaceuta na koncesiju za novu apoteku.

ZAKLJUČCI

Iz analize situacije vezane za uslove otvaranje petnaeste beogradske apoteke može se zaključiti da je država imala velikog uticaja u dostupnosti apoteka, dostupnosti farmaceuta i dostupnosti lekova, te da je uticala na uspostavljanje apotekarske mreže u Srbiji s početka XX veka, usled čega je došlo i do razvoja usluga zdravstvene zaštite

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KLJUČNE RIJEČI: koncesija, konkurs, apoteka, apotekarska mreža

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EXPENDING PHARMACY NETWORK: ON THE TRACE OF THE ADVERTISEMENT FOR OPENING THE 15TH BELGRADE PHARMACY AT THE BEGINNING OF THE 20TH CENTURY

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INTRODUCTION AND OBJECTIVE
Economic development and population growth in Serbia at the beginning of the 20th century made an impact to increase the need of opening new public pharmacies in Serbia , especially in the cities . According to the Law on Medical Profession and Public Health Protection, the Ministry of Internal Affairs determined exactly the area and place for opening a pharmacy. The paper is aimed to display and analyse the role of Serbian state in establishing public pharmacies' network by presenting an advertisment made for opening the 15th public pharmacy in Belgrade.

METHODS
This paper is based on the historical method and documentary analysis of primary and secondary data sources.

RESULTS
Until 1930s, there were two types of concessions for opening public pharmacies in Serbia: a) on the basis of "real law", if the pharmacy owner was not a professional, and b) on the basis of "personal right", under which a pharmacy could be opened or held exclusively by a person of Serbian nationality who acquired the master of pharmacy degree (M.S.) or the doctor of phylosophy in pharmacy degree (PhD), or a foreigner who will receive Serbian citizenship within a year [1]. The Ministry of Internal Affairs regulated the expanding of pharmacies' network in Serbia through the planned granting of concessions with clearly defined areas and places for opening pharmacies. On June 3, 1906, it was announced a competition for opening the 15th public pharmacy in Belgrade. Out of ten inland pharmacists who planned to move their pharmacies to Belgrade only the pharmacist Velimir Karic was granted the right to open a pharmacy in the "Savinac" area, as the owner of pharmacy in Vranje with the greatest experience gained in pharmacy practice [2]. The process of obtaining a pharmacy license in Belgrade raised a number of questions on the right to grant a new concession to pharmacists who wanted to alienate or return existing ones. The Ministry of Internal Affairs, by the right of supreme supervision, regulated the issue of areas, places and pharmacists' rights to receive a concession for a new pharmacy.

CONCLUSIONS
From the analysis of the situation related to terms for founding the 15th public pharmacy in Belgrade, there are substantial evidences that Serbian state had a great impact on the accessability of community pharmacies and medicines, which influenced the pharmacy network in Serbia to be established and expended at the beginning of the 20th century. Accordingly Serbian healthcare services were also developed.

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KEY WORDS: concession, competition, pharmacy, pharmacy network

Acknowledgment: *The work of DK is carried out under the Project funded by the Ministry of Education, Science and Technological Development of the Republic of Serbia, Grant Number 41004.*

POSTER

STRUKTURA, INFORMIRANOST I MIŠLJENJE KORISNIKA O BILJNIM PREPARATIMA U REPUBLICI HRVATSKOJ

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UVOD I CILJ

Na tržištu postoji veliki broj različitih biljnih preparata koji se razlikuju prema namjeni, kvaliteti i sigurnosti primjene. Cilj istraživanja provedenog u sklopu ovog rada bio je istražiti strukturu korisnika biljnih preparata te njihovo znanje i mišljenje o proizvodima koje koriste. Nadalje, željelo se ispitati u kojoj su mjeri upoznati s razlikama između biljnih lijekova i dodataka prehrani.

METODE

Istraživanje je provedeno u ljekarnama na području Republike Hrvatske. U istraživanje su uključeni korisnici koji su upravo kupili biljni preparat. Od ukupno 20 pitanja jedno pitanje je bilo otvorenog, a 19 zatvorenog tipa. Prvi dio anketnog listića sadržavao je pitanja kojima se ispitala struktura korisnika biljnih preparata dok su u drugom dijelu bila pitanja vezana uz kupljeni biljni preparat. Treći dio ankete sadržavao je pitanja kojima se željelo istražiti koliko su korisnici upoznati s razlikom između biljnih lijekova i biljnih dodataka prehrani. Ostatak pitanja se odnosio na ispitivanje općenitog mišljenja o biljnim preparatima vezano uz njihovu namjenu, kvalitetu i sigurnost primjene.

REZULTATI

Na temelju 562 ankete može se zaključiti da su korisnici nedovoljno informirani o značajkama biljnih preparata koje primjenjuju, te da većina nije svjesna razlike između biljnih lijekova i dodataka prehrani. Većina ispitanika smatra kako biljni pripravci ne mogu imati štetne nuspojave niti stupiti u interakcije s konvencionalnom terapijom kao i da se tijekom primjene biljnih preparata nije potrebno savjetovati sa zdravstvenim djelatnicima. Najpouzdanijim izvorom informacija ispitanici su smatrali ljekarnika.

ZAKLJUČCI

S obzirom na dobivene rezultate uviđa se potreba za boljom edukacijom korisnika kako bi se smanjio rizik od nepravilne primjene te pojave neželjenih posljedica biljnih pripravaka. Pozitivno je da ispitanici prepoznaju ljekarnika kao zdravstvenog djelatnika koji im može pružiti ispravne informacije i potrebne savjete o pravilnoj i sigurnoj primjeni biljnih lijekova i dodataka prehrani.

KLJUČNE RIJEČI: biljni lijek, biljni dodatak prehrani, nuspojave, interakcije, ljekarnik

STRUCTURE, KNOWLEDGE AND OPINION OF USERS ON HERBAL PRODUCTS IN THE REPUBLIC OF CROATIA

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INTRODUCTION AND OBJECTIVE
There are a number of different herbal preparations on the market that differ in purpose, quality and safety of use. The aim of the research was to investigate the structure of users of herbal preparations, as well as their knowledge and opinion about the products they use. Furthermore, the extent to which they were aware of the differences between herbal medicines and dietary supplements was examined.

METHODS
The study was conducted in Croatian pharmacies. The study included users who just purchased an herbal preparation. The form comprised of 19 open- and one closed-type questions. The first part of the questionnaire contained questions on the structure of herbal preparations users. The second and the third part contained questions on purchased herbal preparation and on how well informed the users were on difference between herbal medicines and herbal supplements, respectively. The remainder of the questionnaire concerned the general opinion on herbal preparations regarding their purpose, quality and safety of use.

RESULTS
Based on 562 questionnaires, it can be concluded that users were not sufficiently informed about the characteristics of the herbal preparations they use. They were unaware of the differences between herbal medicines and dietary supplements. Most respondents felt that herbal preparations cannot have harmful side effects or interact with conventional therapy. Furthermore, they thought that it is not necessary to consult healthcare professional when considering the use of herbal preparations. However, the pharmacist was considered the most reliable source of information.

CONCLUSIONS
There is a need for better education on herbal preparation users in order to reduce the risk of improper use and the unintended consequences of such use. It is positive that the users recognize the pharmacist as a healthcare professional who can provide them with the correct information and necessary advice on the proper and safe administration of herbal medicines and supplements.

KEY WORDS: herbal medicines, herbal supplements side effects, interactions, pharmacist

POSTER

FARMACIJA U XVIII I RANOM XIX STOLJEĆU

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UVOD I CILJ

Za farmaciju u XVIII i ranom XIX stoljeću, su vezana mnogobrojna naučna dostignuća, značajna imena naučnika koji su svojim radom i istraživanjem doprinijeli razvoju farmacije, kako pronalaskom novih hemijskih jedinjenja tako i pronalaskom ljekovitih tvari biljnog porijekla [1].

METODE

Saznanja o dostignućima hemičara, ljekara i biologa tokom XVIII i XIX stoljeća, kao i uticaj koji su oni imali na razvoj i poboljšanje farmaceutske prakse prikupljena su istraživačkom metodom.

REZULTATI

Joseph Priestley (1733-1804) je bio engleski znanstvenik, svećenik, političar i filozof. Počeo je eksperimentisati sa ugljikovim dioksidom. Objavio je šest knjiga i više od desetak članaka u kojima opisuje svoje eksperimente i zapažanja o različitim vrstama gasova [1]. Lavoisier (1743 –1794) je transformisao hemiju izoliravši i imenuvši kisik. Njegovi doprinosi su veliki i značajni a posebno se izdvajaju *Priroda sagorijevanja* i *Zakon održanja mase.* Louis Nicolas Vanquelin (1763–1829) je francuski predstavnik apotekara/hemičara XVIII stoljeća. Njegova otkrića su otvorila put ka hemiji alkaloida [1]. Carl Wilhelm Scheele (1742- 1786) bio je švedski farmaceut i hemičar. Poznat je još i pod nadimkom „nesretni Scheele" jer je do velikog broja hemijskih otkrića došao prije drugih, ali u najvećem broju slučajeva zasluge za ta otkrića dobili su drugi naučnici [1]. Na osnovu istraživanja Friedrich Wilhem Adam Sertürner-a, mladog njemačkog apotekara, je iz osušenog soka nezrelih čahura maka *(Papaver somniferum),* kao njegovog prirodnog aktivnog sastojka, izolovan morfij. Primjenu je našao u medicini kao narkotik, analgetik i sedativ. Ime je dobio 1817. godine prema grčkom bogu sna Morpheus-u [1].

ZAKLJUČCI

XVIII stoljeće nije imalo ključnu ulogu u razvijanju farmacije i dalje napredovanje farmacije kao zasebne grane zdrastvenih nauka. Dolazak i razvoj hemije alkaloida je također ubrzalo razvitak farmaceutske industrije. Implementacijom saznanja prirodnih nauka, farmaceuti počinju da iz postojićih sirovina za proizvodnju preparata izoluju aktivne principe, što je označilo masivan napredak u farmakoterapiji.

LITERATURA

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KLJUČNE RIJEČI: razvoj farmacije, alkaloidi, opijum, morfij

PHARMACY OF XVIII AND EARLY XIX CENTURY

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INTRODUCTION AND OBJECTIVE

Relating to the pharmacy of XVIII and early XIX century are many scientific achievements, significant names whose work contributed to the development of pharmacy, with the discovery of new chemical compounds and plant-originating drugs [1].

METHODS

The knowledge about the achievements of chemists, doctors and biologists throughout the XVIII and XIX centuries, as well as the impact they had on the development and improvement of pharmaceutical practice were collected using research methods.

RESULTS

Joseph Priestley (1733-1804) was an english scientist, priest, politician and philosopher. He began by experimenting with carbon dioxide. He has published books and articles in which he explains his experiments and observations about the different types of gas [1]. Lavoisier (1743 -1794) has transformed chemistry by isolating and identifying oxygen. His contributions are large, especially *Oxygen Theory of Combustion* and *The Law of Conservation of Mass.* Louis Nicolas Vanquelin (1763-1829) was a french representative of pharmacists and chemists in the XVIII century. His discoveries have opened the way to alkaloid chemistry [1]. Carl Wilhelm Scheele (1742- 1786) was a swedish chemist and pharmacist. He is known under the nickname "hard-luck Scheele" because he should be credited for a large number of chemical discoveries; in most cases, credits came to other scientists. Morphine was isolated based on the research of Friedrich Wilhelm Adam Sertürner, a german pharmacists. It is used in medicine as a narcotic, analgesic and sedative. It was named in 1817 from *Morpheus*, the Greek god of sleep [1].

CONCLUSIONS

XVIII century had a key role in the development and further advancement of pharmacy as a separate branch of Health science. The development of Alkaloid chemistry has also influenced the pharmaceutical industry. By implementing the findings of natural science, pharmacists began isolating active principles using existing raw materials, which made advances in pharmacotherapy.

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KEY WORDS: pharmacy development, alkaloids, opium, morphine

POSTER

SPORT I FIZIČKA AKTIVNOST MLADIH FARMACEUTA REPUBLIKE SEVERNE MAKEDONIJE

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UVOD I CILJ

U poslednjih nekoliko godina važnost sporta i fizičke aktivnosti (FA) u prevenciji i upravljanju mnogih bolesti i stanja (kardiovaskularnih, metaboličkih, raka itd) dobija sve veći značaj. Ova studija ima za cilj da proceni i podigne svest mladih farmaceuta o važnosti sporta i fizičke aktivnosti i potstakne najbolju praksu kod farmaceuta i savetovanju njihovih pacijenata.

METODE

Istraživanje je obuhvatilo 74 mlada farmaceuta (24 muškaraca i 50 žena), koji su nedavno diplomirali na Farmaceutskom Fakultetu u Skoplju, starosti od 24 - 29 godina, sprovedeno u periodu Februar – Juni 2019 u Kliničkoj Apoteci, Skopje. Upitnik se sastojao od 7 prilagođenih pitanja iz Specijalnog Eurobarometra [1].

REZULTATI

Skoro polovina mladih farmaceuta vežba ili se bavi sportom redovno ili sa određenom redovnošću, 35% nikada, dok 17% retko. 40% ispitanika se bavi drugim FA (kao biciklizam) najmanje jednom nedeljno, dok 34% nikada. Mladi muškarci se bave sportom ili vežbaju značajno više (55%) od mladih žena (36%). Većina farmaceuta (71%) pešači najmanje 10 minuta četiri puta nedeljno ili više. Međutim, 8% uopšte ne pešači. 67% ispitanika troši između 2.5 i 8.5 sati u sedenju dnevno, 17% sedi više od 8.5 sati, a 14% 2.5 sata ili manje. Sport ili FA najčešće se odvija u centrima za zdravlje ili fitnes centrima (32%), u sportskim centrima (25%), kod kuće (19%), u parkovima, na otvorenom (15%). Najčešći razlozi za angažovanje u sportu ili u FA su poboljšanje zdravlja (60%), kondicije (43%), fizičkih performansi (35%), opuštanje (28%) i zabava (25%). Nedostatak vremena je daleko glavni razlog za slabu FA (60%).

ZAKLJUČCI

Poruka o važnosti sporta i FA za održavanje dobrog zdravla i dobrobiti još uvek nije stigla u dovoljnoj meri do mladih farmaceuta u Makedoniji u svojstvu promotora individualnog zdravlja.

LITERATURA

[1] Special Eurobarometer 472, Sport and physical activity, March 2018, doi:10.2766/599562 http://eose.org/wp-content/uploads/2018/03/ebs_472_en.pdf

KLJUČNE RIJEČI: sport, fizička aktivnost, farmaceuti, zdravlje

SPORT AND PHYSICAL ACTIVITY IN YOUNG PHARMACISTS OF THE REPUBLIC OF NORTH MACEDONIA

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BACKGROUND AND OBJECTIVE
In recent years, the importance of sport and physical activity (PA) in prevention and management of many diseases and conditions (cardiovascular, metabolic, cancers etc.) acquired greater prominence. This study aims to evaluate and increase awareness about importance of sport and PA and encourage best practices among pharmacists and counseling their patients.

METHODS
A survey among 74 (24 males and 50 females) young pharmacists who recently graduated on University of Pharmacy in Skopje, aged 24 - 29 years was conducted during February - June 2019 at the Clinical Pharmacy, Skopje. The questionnaire consisted of seven questions adapted from Special Eurobarometer [1].

RESULTS
Almost half of young pharmacists exercise or play sport regularly or with some regularity, 35% never do, while 17% do seldom. 40% of respondents do other PA (like cycling) at last once a week, while 34% never do at all. Young man, play sport or exercise considerable more (55%) than young women (36%). Most pharmacists (71%) walked for at least 10 minutes four time a week or more. However, 8% did not do at all. 67% of respondents spend between 2.5 and 8.5 hours sitting daily, 17% sit for more than 8.5 hours and 14% 2.5 hours or less. Sport or PA most commonly takes place in health or fitness centre (32%), sport centre (25%), at home (19%), in parks and outdoors (15%). The most common reasons for engaging in sport or PA are to improve health (60%), fitness (43%), physical performance (35%), relaxing (28%) and having fun (25%). A lack of time is by far the main reason for lack of PA (60%).

CONCLUSIONS
The message about the importance of sport and physical activity for maintaining good health and well-being has still not got sufficiently to young pharmacists in Macedonia as promoters of individual' health.

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KEY WORDS: sport, physical activity, pharmacists, health

POSTER

UTICAJ FARMACEUTA NA PODIZANJE SVESTI RODITELJA O VAKCINACIJI PROTIV MORBILA, RUBELE I PAROTITISA

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UVOD I CILJ

Male boginje su još uvek vodeći uzrok smrti u nevakcinisane dece, nose najveći globalni rizik. Dobar kolektivni imunitet zahteva 95% vakcinisanog stanovništva. Ovaj rad ima za cilj da predloži način za animaciju roditelja da izgrade pozitivan stav prema imunizaciji svoje dece čime bi se obezbedio i solidan kolektivni imunitet.

METODE

Zdravstveno osoblje uključeno u preventivnom zdravstvenom sistemu mora sprovoditi pozitivan individualni pristup prema svim roditeljima. Efikasne komunikaciske veštine farmaceuta u obrazovnom timu su ključ za sticanje poverenja, koristeći pri tome relevantne zdravstvene studije koje potvrđuju prednosti MRP (morbili, rubela, parotitis) vakcinacije i odgovarajući na sva relevantna pitanja, uključujući rizike i nuspojave vakcine.

REZULTATI

Makedonija pripada zemljama visokog rizika u pogledu epidemija malih boginja zbog trenda smanjenja pokrivenosti imunizacije. U periodu 2010 – 2013 godine vakcinisano je 98.1% populacije, zatim stopa pada na 93.3% u 2014 godini, 88.8% u 2015 godini i na samo 82.1% i 82.6% u 2016 i 2017 godini respektivno[1]. Kao posledica anti-vakcinalne kampanje u Makedoniji, objavljene su tri epidemije: u periodu 2010 – 2011 godine 701 slučaj, u 2014 godini 116 slučaja i 1879 slučaja u još uvek aktuelnoj epidemiji [2]. Statistička obrada podataka porvđuje nizak obuhvat MRP vakcinacijom u Makedoniji i pojavu epidemija malih boginja, što se odražava na ukupnu situaciju u regionu i Evropi, naglašavajći potrebu za pojačano sprovođenje aktivnosti, uključujući informisanje, edukaciju i komunikaciju sa javnošću, posebno sa roditeljima. Roditelji kojima se pristupi na ovakav način retko odbijaju vakcinaciju.

ZAKLJUČCI

Sticanje poverenja roditelja o MRP vakcinaciji je jedini način za efikasnu zaštitu od malih boginja i sprečavanje epidemija. Uticaj farmaceuta u ovom kontekstu, uz upotrebu jahih dokumentiranih argumenata u korist redovnog vakcinisanja je jedan od načina da se obezbedi solidan kolektivni imunitet.

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KLJUČNE RIJEČI: MRP vakcinacija, epidemija, farmaceut, roditelji

FORMAT IZLAGANJA
POSTER

SESIJA: Socijalna farmacija i zakonodavstvo

IMPACT OF PHARMACIST ON RAISING PARENTS' AWARENESS ABOUT MEASLES – RUBELLA – PAROTITIS VACCINATION

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BACKGROUND AND OBJECTIVE
Measles is still the leading cause of death in unvaccinated children, carrying the greatest global burden. A good collective immunity necessitates 95% of the population to be immunized. This paper aims to find ways to animate parents to build a positive attitude towards immunization and provide a solid herd immunity.

METHODS
The health staff involved in the preventive health care system must implement a positive individual approach with all parents. Effective communication skills of the pharmacists in the education team are key to gaining the confidence of parents, using relevant health studies that confirm the benefits of the MRP (measles, rubella, parotitis) vaccination and answering pertinent questions, including the risks and side effects of vaccines.

RESULTS
Macedonia is among the high-risk countries for an epidemic of measles due to a trend of reduced coverage of immunization. In 2010 – 2013, 98.1% of the population was vaccinated, a rate that dropped to 93.3% in 2014, 88.8% in 2015. and to just 82.1% and 82.6% in 2016. and 2017. respectively [1]. As a consequence of anti-vaccination campaigns in Macedonia, three epidemics were declared: in 2010 - 2011 701 cases, in 2014. 116 cases and 1879 cases in the current outbreak [2]. Static data processing confirms a low MRP vaccination coverage in Macedonia and an epidemic of measles, reflecting the overall situation in the region and Europe, emphasizing the need for enhanced enforcement activities, including information, education and communication with the public, especially parents. Parents approached in this way rarely refuse vaccination.

CONCLUSIONS
Gaining the parents' trust about the MRP vaccination is the only way to effectively protect against measles and prevent an epidemics. The impact of the pharmacist in this context using documented strong arguments in favor of regular vaccination is the only way to provide a solid herd immunity.

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KEY WORDS: MRP vaccination, epidemic, parents' awareness

PRESENTATION FORMAT
POSTER

SESSION: Social Pharmacy and legislation

POSTER

TROŠKOVI LIJEČENJA MULTIPLE SKLEROZE U BOSNI I HERCEGOVINI

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UVOD I CILJ

Multipla skleroza (MS) je neurodegenerativno oboljenje koje ostavlja teške posljedice kako za pacijenta tako i za cjelokupno društvo. Procjenjuje se da u BiH boluje oko 3000 pacijenata.[1] Studije koštanja bolesti provode se u cilju procjene direktnih i indirektnih troškova i služe kao alat u donošenju odluka u zdravstvu uključujući i finansiranje lijekova.[2] Korištenjem nalaza ovakvih studija moguće je lakše donijeti odluke o finansiranju lijekova i povećanje njihove dostupnosti pacijentima. Cilj ovog istraživanja bio je definisati troškove mulitple skleroze u BiH na godišnjem nivou i odrediti opterećenje bolesti za pacijenta i društvo.

METODE

Studija je koristila metodu prevalence i sa dna prema vrhu. Podaci su prikupljeni pomoću posebno razvijenog upitnika intervjuisanjem pacijenata i uključili su sve troškove vezane za MS. Pacijenti su praćeni kroz tri posjete u toku jedne godine. Jedinični troškovi su preuzeti iz zvaničnih izvora. Troškovi MS prikazani su iz perspektive društva na godišnjem nivou stratificirano prema vrsti korištene terapije.

REZULTATI

U Tabeli 1 dat je sumarni prikaz direktnih troškova. Ne postoji razlika dijagnostičkih troškova i specijalističkih pregleda unutar posmatranih grupa. Troškovi hospitalizacije najveći su kod pacijenata liječenih kortikosteroidima. Troškovi lijekova najveći su kod onih liječenih modenim terapijama. Kada su u pitanju indirektni troškovi vezani za gubitak produktivnosti zbog prijevremenog penzionisanja oni iznose 27,86.1 BAM, a troškovi bolovanja 1,233.8 BAM po pacijentu godišnje. Ekstrapolacijom ovih troškova na nivo BiH troškovi MS iznose 124,8 miliona BAM.

TABELA 1: *Direktni medicinski troškovi po terapijskim grupama*

Vrsta troška I terapijska grupa	N	Min.	Max.	Percentile			
				25th	50th (Median)	75th	p*
Direktni troškovi dijagnostike (ukupni)							
DMD	33	0.0	1,728.4	644.2	849.2	1,071.3	0.497
CT	20	0.0	3,431.2	86.4	591.4	1,087.7	
NT	9	0.0	1,712.3	151.9	858.2	936.6	
Direktni troškovi medicinskih usluga (ukupni)							
DMD	33	387.6	2,891.3	497.7	571.1	644.5	0.062
CT	20	497.7	1,069.8	571.1	607.8	754.6	
NT	9	461.0	2,219.5	466.0	497.7	607.8	
Direktni troškovi hospitalizacije i medicinskih usluga (ukupni)							
DMD	33	461.0	6,127.8	580.3	1,147.9	2,029.9	0.001
CT	20	1,517.2	7,146.0	2,210.5	3,275.4	4,560.4	
NT	9	1,163.0	3,763.9	1,413.5	1,761.3	2,907.9	
Direktni troškovi lijekova (ukupno)							
DMD	33	17,401.0	26,725.0	19,198.8	20,442.1	22,659.4	0.001
CT	20	3,564.0	23,616.0	5,529.0	7,884.0	10,224.0	
NT	9	1,800.0	25,080.0	4,500.0	6,540.0	13,920.0	
Direktni troškovi lijekova za MS (ukupni)							
DMD	33	15,925.0	17,424.0	15,925.4	16,662.1	17,398.8	0.001
CT	20	2,484.0	2,484.0	2,484.0	2,484.0	2,484.0	
NT	9	0.0	0.0	0.0	0.0	0.0	
Direktni troškovi (ukupni)							
DMD	33	34,803.0	53,451.0	38,397.6	40,884.2	45,318.7	0.0001
CT	20	7,128.0	47,232.0	11,058.0	15,768.0	20,448.0	
NT	9	3,600.0	50,160.0	9,000.0	13,080.0	27,840.0	

**Krusekal WallisTest*
DMD lijekovi koji mijenjanju tok bolesti

ZAKLJUČCI

Ova studija predstavlja dubinsku analizu ukupnih troškova MS iz društvene perspektive oslikavajući ekonomsko opterećenje koje nosi MS u BiH. Iako studije koštanja boilesti ne mogu biti korištene za procjenu troškovne efektivnosti pojedinih terapijskih opcija, rezultati ovakvih studija daju značajne informacije za buduće pojedinačne analize i mogu poslužiti u donošenju odluka o finansiranju novih lijekova.

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KLJUČNE RIJEČI: Multipla skleroza, koštanje bolesti, farmakoekonomika, zdravstvena politika

COST OF MULTIPLE SCLEROSIS TREATMENT IN BOSNIA AND HERZEGOVINA

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INTRODUCTION AND OBJECTIVE

Multiple sclerosis (MS) is neurodegenerative illness with huge health complications not just for the patient but the whole society. It is estimated that there is around 3,000 patients in Bosnia and Herzegovina (B&H).[1] Cost of illness (COI) studies of MS are commonly performed in order to identify direct and indirect cost impact as a potential tool for healthcare decision makers in setting up and prioritizing healthcare policies and interventions that they are supposed to implement and reimburse.[2] Using COI study results could help in drug reimbursement desicisons and its availability. The aim of this research was to identify annual costs related to MS in B&H and its burden for patient and the society.

METHODS

The study used a prevalence-based bottom-up approach. Data were collected by a cross-sectional survey directly from patients, with the objective of including all costs related to MS. Patients have been followed through three visits. Unit costs have been taken from the official sources. Costs of MS are presented from the societal perspective at annual level stratified by treatment used.

RESULTS

In Table 1 summary of direct costs per treatment group are presented. As we can see there is no difference in cost of diagnostic tests and imaging and medical services between treatment groups. Cost of hospitalization are highest among patients treated with corticosteroids. Cost of medicines is highest among DMD treatment group and driven by cost of DMD drugs.

Considering indirect costs related to productivity cost due to early retirement amount of 27,86.1 BAM and cost of sick leave amount 1,233.8 BAM per patient per year. Extrapolating these cost on national level, based on available epidemiology data, cost of MS in Bosnia and Herzegovina annually amount 124.8 million BAM.

Table 1: *Direct medical costs per treatment group (BAM)*

Type of costs and treatment group	N	Min.	Max.	Percentile			p*
				25th	50th (Median)	75th	
Direct cost of medical tests and imaging per treatment group (total)							
DMD	33	0.0	1,728.4	644.2	849.2	1,071.3	0.497
CT	20	0.0	3,431.2	86.4	591.4	1,087.7	
NT	9	0.0	1,712.3	151.9	858.2	936.6	
Direct cost of medical services (total)							
DMD	33	387.6	2,891.3	497.7	571.1	644.5	0.062
CT	20	497.7	1,069.8	571.1	607.8	754.6	
NT	9	461.0	2,219.5	466.0	497.7	607.8	
Direct cost of hospitalization and medical services (total)							
DMD	33	461.0	6,127.8	580.3	1,147.9	2,029.9	0.001
CT	20	1,517.2	7,146.0	2,210.5	3,275.4	4,560.4	
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Direct cost of medicines (total)							
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NT	9	1,800.0	25,080.0	4,500.0	6,540.0	13,920.0	
Direct cost of medicines for MS (total)							
DMD	33	15,925.0	17,424.0	15,925.4	16,662.1	17,398.8	0.001
CT	20	2,484.0	2,484.0	2,484.0	2,484.0	2,484.0	
NT	9	0.0	0.0	0.0	0.0	0.0	
Direct cost (total)							
DMD	33	34,803.0	53,451.0	38,397.6	40,884.2	45,318.7	0.0001
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NT	9	3,600.0	50,160.0	9,000.0	13,080.0	27,840.0	

**Krusekal WallisTest*
disease-modifying drugs; CT koritkosteroidi/corticosteroids; NT bez terapije/no treatment

CONCLUSIONS

This study provides an in-depth analysis of the total societal and payer perspective costs in Bosnia and Herzegovina for MS illustrating the burden of disease. Provided data are important for the development of health policies. Although COI studies cannot be used to assess the cost-effectiveness of specific treatment, the results of this study provide significant information for future cost-effectiveness evaluations of new therapeutic options in MS during reimbursement process in Bosnia and Herzegovina.

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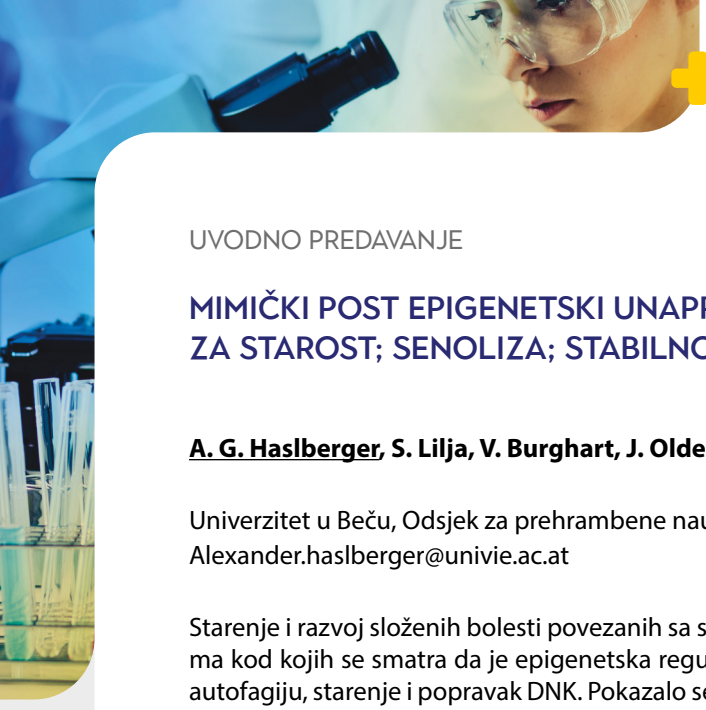
KEY WORDS: Multiple sclerosis, cost-of-illness, pharmacoeconomics, health policy

BROMATOLOGIJA I NUTRICIJA



UVODNO PREDAVANJE

MIMIČKI POST EPIGENETSKI UNAPREĐUJE SASTAV MIKROBIOTE; UPALE VEZANE ZA STAROST; SENOLIZA; STABILNOST DNA I MARKERI STARENJA

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Starenje i razvoj složenih bolesti povezanih sa starenjem kontrolira se obilježavanjem molekularnih mehanizama kod kojih se smatra da je epigenetska regulacija uključena u regulaciju atricije telomera, ekspresiju gena, autofagiju, starenje i popravak DNK. Pokazalo se da post, ali i biljni sastojci poput antocijana, EGCG, spermidina moduliraju epigenetsku regulaciju ovih mehanizama modificiranjem puta AMPK, SIRT i mTOR. Nadalje, butirat dobijen iz mikrobiota i BHB imaju snažne učinke na epigenetsku metilaciju, histonsku deacetilaciju i miRNA.

Analizirali smo markere starenja kao što su dužina telomera, mitohondrijalni DNA, ekspresija IL6, TNFa, epigenetska metilacija DNK i miRNA, razbijanje DNK i popravljanje DNK, sastav GI mikrobiote, kao i autofagija i senoliza u modelima ljudskih ćelija i prehrana s visokim udjelom masti kod miševa. Učinci epigenetskih aktivnih dodataka analizirani su u kapi krvi kohorte volontera. Metilacija DNA i mikroRNA analizirani su pomoću HRM qPCR, a ekspresija gena pomoću RT PCR ili NGS. Pucanja DNA analizirana su Cometovim testom. Promjene sastava mikrobiote analizirane su pomoću NGS-a baziranom na Nanoporu. Dodaci uključuju injekcije s visokim EGCG ili biljnim sastojcima koji aktiviraju sirtuin.

Prehrana s visokim udjelom masti uzrokovala je veliki broj pucanja DNK u raznim tkivima što se može značajno smanjiti postom, EGCG-om, galijskom kiselinom kod miševa. Prehrana bogata polifenolom povećala je ekspresiju enzima za popravak DNK MLH1 i prebacila GI mikrobiotu prema korisnom fenotipu kojim dominira *Prevotella*. In vitro i istraživanje na ljudima, uključujući piće s visokim udjelom EGCG, pokazalo je povećanu dužinu telomera u korelaciji s izmijenjenim promjenama cMYC-a i hTERT-a, te poboljšane epigenetske markere starenja. Poboljšana je ekspresija mikroRNA koja se odnosi na upalu. EGCG i butirat pokazuju značajne učinke starenja izazvanog BRDU-om u fibroblastima i na ekspresiju gena koji su relevantni za autofagiju i starenje.

Zaključno, prehrana s postom koja potiče ketogenezu i proizvodnju masnih kiselina kratkog lanca, kao i aditivi u hrani koji modificiraju puteve SIRT-a i mTOR-a, obećavaju poboljšanje zdravog starenja i zaštite zdravlja posebno za bolesti povezane s metabolizmom. Potpuna provedba individualizirane, preventivne zdravstvene zaštite, analiza starenja i epigenetskih parametara mogla bi pomoći u vođenju individualizirane zaštite zdravlja.

FASTING MIMETICS EPIGENETICALLY IMPROVE GUT MICROBIOTA COMPOSITION; AGE-RELATED INFLAMMATION; SENOLYSIS; DNA STABILITY AND AGING MARKERS

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Aging and the development of age-related complex diseases is controlled by a hallmark of molecular mechanisms where epigenetic regulation is considered to be involved in the regulation of telomere attrition, gene expression, autophagy, senescence and DNA repair. Fasting, but also plant ingredients such as anthocyans, EGCG, spermidine have been shown to modulate epigenetic regulation of these mechanisms by modification of AMPK, SIRT and mTOR pathways. Furthermore, microbiota-derived butyrate and BHB have strong effects on epigenetic methylation, histone deacetylation and miRNAs.

We analyzed markers for aging such as telomere length, mitochondrial DNA, expression of IL6, TNFa, epigenetic DNA methylation and miRNAs, DNA breaks and DNA repair, GI microbiota composition as well as autophagy and senolysis in human, cell models, and high fat diet mouse model. Effects of epigenetic active supplements were analyzed in blood drops of cohorts of human volunteers. DNA methylation and microRNA were analyzed by HRM qPCR and gene expression by RT PCR or NGS. DNA breaks were analyzed by Comet assay. Changes of the composition of microbiota were analyzed by Nanopore-based NGS. Supplements included shots with high EGCG or sirtuin-activating plant ingredients.

Hight fat diet induced high amounts of DNA breaks in various tissues which could be significantly reduced by fasting, EGCG, gallic acid in mice. A polyphenol rich diet increased expression of DNA repair enyzyme MLH1 and shifted GI microbiota towards a beneficial *Prevotella* dominated phenotype. In vitro and in a human study including a drink with high EGCG content we found increased length of telomers correlating with altered changes of cMYC and hTERT, and improved epigenetic markers of aging. Expression of microRNAs related to inflammation were improved. EGCG and butyrate shows significant effects of BRDU induced senescence in fibroblasts and on expression of genes with relevance for autophagy and senescence.

In conclusion, fasting diets which induce ketogenesis and production of short chain fatty acids as well as food additives which modify SIRT and mTOR pathways hold the promise to improve healthy aging and health prevention especially for metabolic related diseases. To fully implement an individualized, preventive health care, analysis of aging and epigenetic parameters could help to guide an individualized health prevention.

UVODNO PREDAVANJE

ANTIOKSIDANSI U PREVENCIJI I TERAPIJI METABOLIČKOG SINDROMA

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Metabolički sindrom predstavlja udruženost metaboličkih poremećaja (abdominalna gojaznost, hiperglikemija, hipertenzija i aterogena dislipidemija) koji povećavaju rizik za nastanak kardiovaskularnih bolesti i dijabetesa tipa 2. Etiologija je složena i temelji se kako na genetskim činiocima, tako i na životnim navikama pojedinaca. Pravilna ishrana uz fizičku aktivnost predstavlja osnovu nefarmakoloških mjera u prevenciji i liječenju metaboličkog sindroma, čiji je osnovni cilj tretman gojaznosti, kao i korekcija pridruženih metaboličkih poremećaja.

S obzirom na inverznu povezanost statusa neenzimske antioksidativne zaštite, kao i endogenih koncentracija antioksidativnih vitamina i minerala sa rizikom od nastanka metaboličkog sindroma i njegovih komplikacija, postoji interesovanje za ispitivanjem potencijalnih korisnih zdravstvenih efekata konzumiranja namirnica bogatih dijetarnim antioksidansima, kao i dodataka ishrani. Pored antioksidativnih vitamina i minerala, suplementacija nenutritivnim antioksidansima kao što su alfa-lipoinska kiselina, koenzim Q10, karotenoidi, polifenoli (npr. kurkumin, resveratrol, kvercetin) i dr., pojedinačno ili u kombinaciji, takođe može da bude od značaja. Iako *in vitro* istraživanja, studije na eksperimentalnim životinjama, kao i pojedine kliničke studije, ukazuju na potencijalni klinički značaj antioksidanasa u tretmanu metaboličkog sindroma, rezultati velikih randomizovanih kliničkih istraživanja i meta-analize su nekonzistentni. Izostanak potvrde očekivanog pozitivnog djelovanja antioksidanasa u istraživanjima koja uključuju veliki broj ispitanika, može se objasniti odsustvom adekvatnih biohemijskih markera za procjenu oksidativno-stresnog statusa ispitanika pre i tokom intervencije, zatim problemima vezanim za definisanje optimalnih doza i dužine trajanja intervencije, kao i potencijalnih interakcija sa farmakološkom terapijom.

U nedostatku dovoljno čvrstih dokaza o korisnim efektima suplementacije antioksidansima, osobama sa metaboličkim sindromom se preporučuje konzumiranje svježeg voća, povrća, nerafinisanih žitarica i drugih dijetarnih izvora antioksidanasa, uz isticanje značaja njihovog sinergističkog i aditivnog djelovanja. Bolje razumjevanje složenih etiopatogenetskih mehanizama, zatim mehanizama regulatornog djelovanja antioksidanasa, kao i njihovih interakcija sa crijevnom mikrobiotom, može dovesti do razvoja individualnih preventivnih i terapijskih pristupa primjene antioksidanasa u tretmanu metaboličkog sindroma.

KLJUČNE RIJEČI: metabolički sindrom, antioksidansi, mikronutrijenti, biološki aktivni sastojci

ANTIOXIDANTS IN THE PREVENTION AND TREATMENT OF METABOLIC SYNDROME

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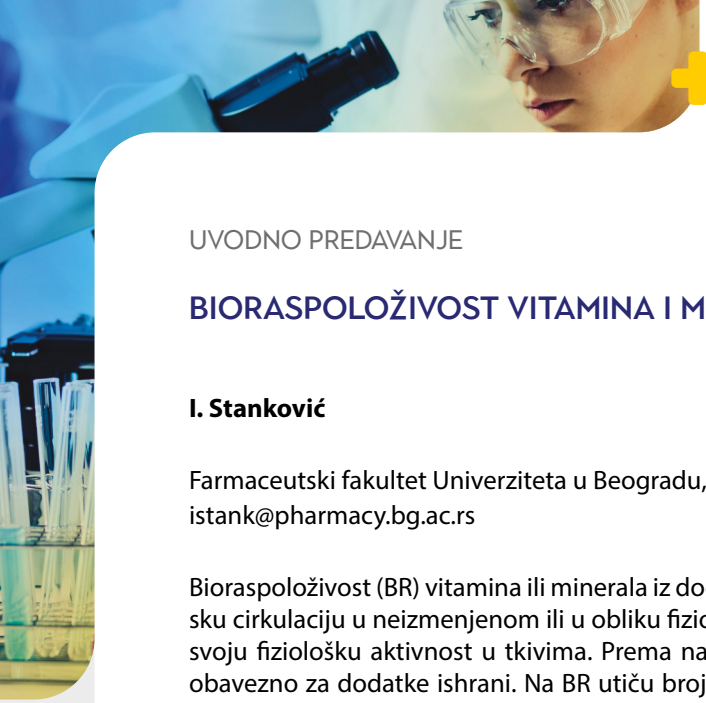
Metabolic syndrome (MetS) is a constellation of abnormalities such as abdominal obesity, hyperglycemia, hypertension and atherogenic dyslipidemia which increase the risk for cardiovascular disease and type 2 diabetes mellitus. Etiology of the MetS is complex, and it is based on genetic, as well as environmental factors. The balanced diet and increased physical activities are essential parts of the management of the MetS and its components.

Based on the inverse correlation between total antioxidant status, as well as antioxidant plasma vitamin and mineral levels with risk of the MetS and its complications, there have been raising interest in the study of the health effects consuming food rich in antioxidants, as well as antioxidant supplements. In addition to antioxidant vitamins and minerals, other non-nutritive antioxidants may exert beneficial effects like alpha-lipoic acid, coenzyme Q10, carotenoids, polyphenols, like curcumin, resveratrol, quercetin and others, single or in combinations.

Some *in vitro* studies, animal models, and a limited number of clinical studies support the benefits of antioxidants by counteracting the effects of many metabolic risk factors. However, the meta-analysis of clinical trials and prospective cohort studies demonstrate that antioxidant supplementation does not improve clinical outcomes in people with metabolic syndrome. The results from antioxidant intervention studies are difficult to compare because studies vary in the inclusion criteria, the assessed biomarkers and outcomes, antioxidant compounds, doses and duration of intervention. Also, there is a potential risk of antioxidant-drug interactions. Increasing the consumption of fruits, vegetables, whole grains, and other dietary antioxidants sources, due to the proposed synergistic and additive effects of compounds, present the current recommended nutritional strategy to MetS. A further better understanding of etiopathological processes, the possible mechanisms of action of antioxidants, as well as its interactions with gut microbiota, can lead to developing new and individual strategies to MetS treatment.

KEYWORDS: metabolic syndrome, antioxidants, micronutrients, phytonutrients



UVODNO PREDAVANJE

BIORASPOLOŽIVOST VITAMINA I MINERALA IZ DODATAKA ISHRANI

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Bioraspoloživost (BR) vitamina ili minerala iz dodataka ishrani označava koliko je od unete doze došlo u sistemsku cirkulaciju u neizmenjenom ili u obliku fiziološki aktivnih metabolita i odatle može da se raspodeli i ispolji svoju fiziološku aktivnost u tkivima. Prema nacionalnim i propisima Evropske Unije (EU), ispitivanje BR nije obavezno za dodatke ishrani. Na BR utiču brojni faktori među kojima su najznačajniji: formulacija preparata, dezintegracija i rastvorljivost farmaceutskih oblika, kofaktori i inhibitori, ostali sastojci preparat (aditivi i dr), hemijski izvori vitamina i minerala, rastvorljivost, interakcije sa sastojcima hrane, interakcije sa lekovima, presistemski metabolizam, individualni nutritivni ili fiziološki faktori (nutritivni status, starost, bolest) i dr. Generalno, apsorpcija je bolja iz tečnih preparata (rastvori, šumeće tablete, sirupi) nego iz čvrstih farmaceutskih oblika (tablete, kapsule). Ispitivanje dezintegracije i rastvorljivosti su deo GMP ili HACCP sistema proizvođača. Fitinska kiselina gradi sa gvožđem, cinkom, kalcijumom i magnezijumom soli koje se ne apsorbuju. Vlakna smanjuju apsorpciju hidrosolubilnih vitamina i minerala, masti povećavaju apsorpciju liposolubilnih vitamina, a polioli smanjuju BR svih vitamina i minerala (laksativno dejstvo).

U dodacima ishrani dozvoljena je upotreba oko 200 različitih supstanci kao izvora 13 vitamina i 17 minerala. U EU bezbednost i bioraspoloživost dozvoljenih izvora vitamina i minerala evaluira Naučni panel za aditive i nutritivne izvore (ANS) Evropskog autoriteta za bezbednost hrane (EFSA). Tako je npr. BR holekalciferola (vitamin D_3) 1,7 puta veća nego ergokalciferola (vitamin D_2) mereno povećanjem nivoa 1,25-dihidroksi holekalciferola u serumu [1], a BR 1 µg folata iz hrane ekvivalentna je 0,6 µg folne kiseline iz dodataka ishrani, odnosno 0,5 µg folne kiseline iz dodataka ishrani uzetog na prazan želudac [2].

Dodaci ishrani se uglavnom prodaju u apotekama gde je uloga farmaceuta veoma značajna u preporuci ne samo najadekvatnijeg dijetetskog suplementa već i preparata koji sadrži vitamine i minerale visoke bioraspoloživosti.

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KLJUČNE RIJEČI: bioraspoloživost, dodaci ishrani, dijetetski suplementi, vitamini i minerali

BIOAVAILABILITY OF VITAMINS AND MINERALS FROM FOOD SUPPLEMENTS

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The bioavailability (BA) of vitamins or minerals from dietary supplements indicates how much of a given dose has entered the systemic circulation in unaltered or in the form of physiologically active metabolites and from there it can distribute and exert its physiological activity in tissues. According to national and EU regulations, BA testing is not mandatory for food supplements. The BA is influenced by a number of factors, the most important being: formulation of preparations, disintegration and solubility of pharmaceutical forms, cofactors and inhibitors, other constituents of the preparation (additives, etc.), chemical sources of vitamins and minerals, solubility, interactions with food constituents, interactions with drugs, presystemic metabolism, individual nutritional or physiological factors (nutritional status, age, disease), etc. Generally, absorption is better from liquid preparations (solutions, effervescent tablets, syrups) than from solid pharmaceutical forms (tablets, capsules). Disintegration and solubility testing are part of the manufacturer's GMP or HACCP system. Phytic acid forms with iron, zinc, calcium and magnesium salts that are not absorbed. Dietary fibers reduce the absorption of hydrosoluble vitamins and minerals, fat increases the absorption of liposolubile vitamins, and polyols decrease the BA of all vitamins and minerals (laxative effect).

The food supplements allow the use of about 200 different substances as sources of 13 vitamins and 17 minerals. In the EU, the safety and bioavailability of authorized sources of vitamins and minerals are evaluated by the Scientific Panel on Additives and Nutrition Sources (ANS) of the European Food Safety Authority (EFSA). Thus, e.g. BA of cholecalciferol (vitamin D3) is 1.7 times higher than ergocalciferol (vitamin D2) measured by an increase serum 1,25-dihydroxy cholecalciferol [1], and BA of 1 µg of folate from food is equivalent to 0.6 µg of folic acid from food supplements, or 0.5 µg of folic acid from a food supplement taken on an empty stomach [2].

Food supplements are generally sold in pharmacies where the role of the pharmacist is very important in recommending not only the most appropriate food supplement but also a preparation containing vitamins and minerals of high bioavailability.

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KEY WORDS: bioavailability, food supplements, dietary supplements, vitamins and minerals

ORALNA PREZENTACIJA

PLODOVI RODA RIBES - MOĆNI ANTIOKSIDANSI?

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UVOD I CILJ

Bobičasto voće roda Ribizli (*Ribes*) je nativno za umjerene regione Sjeverne Amerike, ali se kultiviše i u našim krajevima. Najčešće vrste koje se i najviše konzumiraju su crvena ribizla (*Ribes rubrum L.*), crna ribizla (*Ribes nigrum L.*)i ogrozd (*Ribes uva-crispa L.*).

Plodovi ovog voća predstavljaju bogate izvore bioaktivnih spojeva: polifenola, antocijana, vitamina C i minerala. Brojne studije su pokazale da je konzumiranje bobičastog voća povezano sa poboljšanjem lipidnog profila, pojačavanjem imunog odgovora i smanjenjem oksidativnog oštećenja na biološkim molekulama, što se pripisuje antioksidansima prisutnim u ovom voću [1]. Danas se zna da je oksidativni stres u osnovi brojnih hroničnih bolesti, uključujući dijabetes, hronične inflamacije, neurodegenerativne bolesti i kancer [2].

Cilj ovog rada bio je da se ispita antioksidativni kapacitet plodova bobičastog voća iz roda Ribizli i to crvene ribizle, crne ribizle i ogrozda, prikupljenih sa područja Sarajeva i Tuzle.

METODE

U eksperimentalnom dijelu ovoga rada određen je sadržaj ukupnih fenolnih spojeva (flavonoida i neflavonoida) u ispitivanim uzorcima primjenom tri spektrofotometrijske metode (Folin- Ciocalteu-ova metoda, vanilin-HCl metoda i kolorimetrijska metoda sa aluminijum (III) hloridom), te određen njihov antioksidativni kapacitet primjenom serije*in vitro* testova (DPPH(2,2- difenil-1-pikrilhidrazil) radikal esej, FRAP (ferric ion reducing antioxidant power assay) esej, TEAC (total antioxidant potential test) esej i određivanje ukupnog antioksidativnog kapaciteta metodom po Prietu i sar. [3]).

REZULTATI

U ispitivanim uzorcima prosječni sadržaj ukupnih fenola iznosio je 320 mg/l (1,62 mg/g uzorka) izražene kao ekvivalent taninske kiseline (TAE), sa dominatnim udjelom neflavonoida (210 mg/l TAE odnosno 1,05 mg TAE/g uzorka). Prosječni sadržaj antocijanidina iznosio je 280 mg/l katehina (1,4 mg katehina/g uzorka), a ukupnih flavonoida 20 mg/l kvercetina (0,1 mg kvercetina/g uzorka). Svi ispitivani uzorci pokazali su veći antioksidativni kapacitet u odnosu na čiste antioksidanse (askorbinska kiselina i katehin).

ZAKLJUČCI

Očekivano isptivani uzorci pokazali su visok sadržaj ukupnih fenolnih spojeva, kao i značajnu antioksidativnu aktivnost.

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[3] Prieto P, Pineda M, Aguilar M. Spectrophotometric quantitation of antioxidant capacity through the formation of a phosphomolybdenum complex: Specific application to the determination of vitamin E. Analyt Biochem. 1999; 269: 337-341.

KLJUČNE RIJEČI: antioksidansi, crvena ribizla, crna ribizla, ogrozd

FRUITS OF THE GENUS RIBES - POWERFUL ANTIOXIDANTS?

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INTRODUCTION AND OBJECTIVE

Berries from the genus *Ribes*are native for the regions with moderate climate in North America, but often are cultivated in our country. The most common species that are also consumed the most are red currant (*Ribes rubrum L.*), black currant (*Ribes nigrum L.*) and gooseberry (*Ribes uva-crispa L.*). These fruits are rich sources of bioactive compounds such as polyphenols, anthocyanins, vitamin C and minerals. Results of numerous studies showed positive correlation between consumption of berries and improvement of lipid profiles, enhancing immune responses and reducing the oxidative damage on biomolecules, which is attributed to antioxidants present in this type of fruit [1]. Nowadays is well known that oxidative stress is involved in etiology of some chronic diseases, including diabetes, chronic inflammation, neurodegenerative disorders and cancer [2].
The main aim of this work was to investigate antioxidant capacity of fruits from the genus *Ribes*, particularly red currant, black currant and gooseberry, harvested in the region of Sarajevo and Tuzla.

METHODS

In experimental part of this study content of total phenolic (flavonoids and non flavonoids) in investigated samples was determined by means of three spectroscopic methods (Folin- Ciocalteu method, vanilin-HCl method and colorimetric method with aluminum (III) chloride), as well as their antioxidant capacity using different *in vitro* test (DPPH (2,2- diphenyl-1-picrylhydrazyl) radical assay, FRAP (ferric ion reducing antioxidant power assay) assay, TEAC (total antioxidant potential test) assay and total antioxidant capacity according to Prietoet all. [3]).

RESULTS

The aerage content of total phenolic was 320 mg/L (1,62 mg/g of sample) expressed as tannic acid equivalent (TAE), dominated by non flavonoids (210 mg/L TAE or 1,05 mg TAE/g of sample). The average content of anthocyanidins was 280 mg/L of catechin(1,4 mg catechin/g of sample) and total flavonoid content 20 mg/L of quercetin (0,1 mg quercetin/g of sample). All investigated samples exhibited higher antioxidant capacity comparing to pure, standard antioxidants (ascorbic acid and catechin).

CONCLUSIONS

As expected, all the samples showed high content of total phenolic, as well as significant antioxidant activity.

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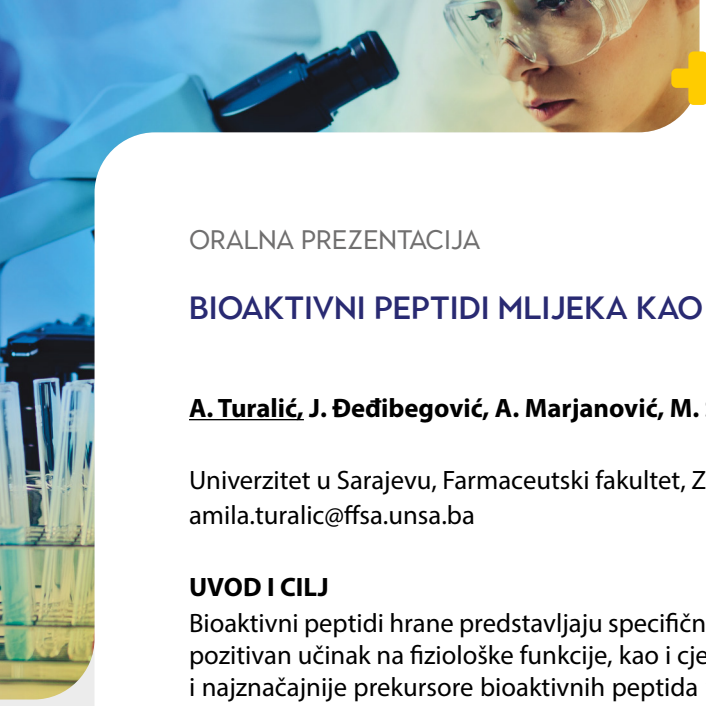
[3] Prieto P, Pineda M, Aguilar M. Spectrophotometric quantitation of antioxidant capacity through the formation of a phosphomolybdenum complex: Specific application to the determination of vitamin E. Analyt Biochem. 1999; 269: 337-341.

KEY WORDS: antioxidants, red currant, black currant, gooseberry



ORALNA PREZENTACIJA

BIOAKTIVNI PEPTIDI MLIJEKA KAO INHIBITORI DIPEPTIDIL-PEPTIDAZE IV

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UVOD I CILJ

Bioaktivni peptidi hrane predstavljaju specifične proteinske fragmente koji pored nutritivne uloge mogu imati pozitivan učinak na fiziološke funkcije, kao i cjelokupno zdravlje. Proteini mlijeka predstavljaju najistraživanije i najznačajnije prekursore bioaktivnih peptida povezanih s povoljnim učincima na kardiovaskularni, gastrointestinalni, endokrini, imunološki i nervni sistem. Brojne studije ukazuju da proteini mlijeka mogu doprinijeti poboljšanju postprandijalnih nivoa glukoze kod zdravih osoba i oboljelih od diabetes mellitus tipa 2 (T2DM), za što bi mogli biti odgovorni bioaktivni peptidi koji inhibiraju enzim dipeptidil-peptidazu IV (DPP-IV). Cilj ovog rada je pregled dosadašnjih saznanja o bioaktivnim peptidima koji djeluju kao DPP-IV inhibitori, s fokusom na peptide mlijeka.

METODE

Izvršen je pregled relevantne literature o bioaktivnim peptidima mlijeka koji djeluju kao DPP-IV inhibitori, njihovoj ulozi i mogućnostima primjene u T2DM.

REZULTATI

Unos proteina mlijeka povezan je sa stimulacijom sekrecije inzulina, povećanjem nivoa inkretina ili smanjenjem aktivnosti enzima uključenih u razgradnju ugljikohidrata, no tačan mehanizam koji objašnjava snižavanje nivoa glukoze nakon njihovog unosa još uvijek nije sasvim razjašnjen.

Iako se ne može sa sigurnošću tvrditi da je snižavanje nivoa glukoze povezano s peptidnim DPP-IV inhibitorima, rezultati istraživanja nedvojbeno ukazuju da *in vitro* razgradnjom proteina mlijeka mogu nastati peptidi s DPP-IV inhibitornim djelovanjem. Kliničke studije koje potvrđuju DPP-IV inhibiciju djelovanjem bioaktivnih peptida još uvijek su nedostatne. Iako su identificirani u gastrointestinalnom traktu, serumu i plazmi, rezultati dosadašnjih istraživanja ukazuju na slabu bioraspoloživost bioaktivnih peptida koja je najvjerovatnije posljedica opsežne razgradnje uslijed djelovanja peptidaza u gastrointestinalnom traktu i cirkulaciji. Stoga je određivanje proteolitičke stabilnosti bioaktivnih peptida jedno od ključnih pitanja u ovom istraživačkom području kako bi se uopšte moglo razmatrati njihovo djelovanje *in vivo* i potencijalna primjena.

ZAKLJUČCI

Budući da su bioaktivni peptidi mlijeka slabiji DPP-IV inhibitori u odnosu na gliptine, cilj njihove potencijalne primjene nije zamjena sintetskih lijekova. Mogli bi pronaći primjenu u sklopu nutritivne strategije za kontrolu glikemije u prediabetesu ili T2DM.

KLJUČNE RIJEČI: mlijeko, diabetes mellitus tipa 2, bioaktivni peptidi, DPP-IV inhibitori

BIOACTIVE MILK PEPTIDES AS DIPEPTIDYL PEPTIDASE IV INHIBITORS

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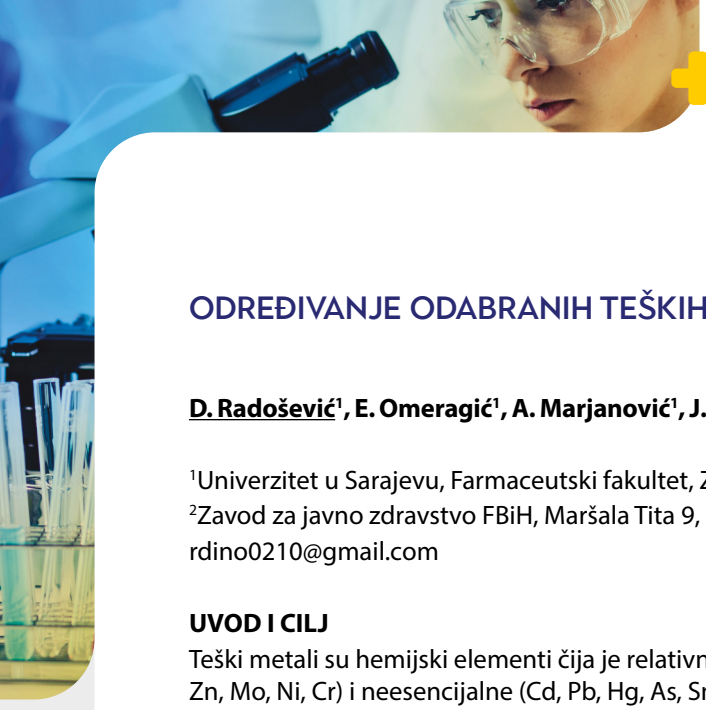
INTRODUCTION AND OBJECTIVE
Food protein-derived bioactive peptides are specific protein fragments that, in addition to their nutritional role, can have a positive impact on physiological functions, as well as overall health. Milk proteins are the most studied and most significant precursors of bioactive peptides associated with beneficial effects on cardiovascular, gastrointestinal, endocrine, immune and nervous system. Numerous studies indicate that milk proteins can contribute to postprandial glucose levels improvement in healthy individuals and type 2 diabetic patients (T2DM), which could be attributed to bioactive peptides that inhibit enzyme dipeptidyl peptidase IV (DPP-IV). The aim of this work is to provide an overview on current knowledge on bioactive peptides that act as DPP-IV inhibitors with major focus on milk peptides.

METHODS
Efforts have been made to review the available information in literature on bioactive milk peptides that act as DPP-IV inhibitors, their role and potential usage in T2DM.

RESULTS
Milk protein intake is associated with stimulation of insulin secretion, an increase in incretin levels or reduced activity of carbohydrate-degrading enzymes, but the exact mechanism that explains the decrease in glucose levels after their intake has not yet been fully elucidated.
Although it cannot be safely argued that glucose lowering is associated with peptide DPP-IV inhibitors, the results of the studies undoubtedly indicate that *in vitro* digestion of milk proteins can result in peptides with DPP-IV inhibitory activity. Clinical studies that definitely confirm the DPP-IV inhibition by bioactive peptides are still inconsistent. Although they are identified in the gastrointestinal tract, serum and plasma, the results of previous studies indicate poor bioavailability of bioactive peptides, which is most likely due to the extensive degradation by peptidases in the gastrointestinal tract and circulation. Therefore, determining the proteolytic stability of bioactive peptides is one of the key topics in this research area in order to consider their *in vivo* activity and potential applications at all.

CONCLUSIONS
Since bioactive milk peptides are weaker DPP-IV inhibitors compared to gliptins, the goal of their potential usage is not synthetic drugs replacement. They could be used as part of nutritional strategy in glycaemia management in prediabetes or T2DM.

KEYWORDS: milk, type 2 diabetes, bioactive peptides, DPP-IV inhibitors



ODREĐIVANJE ODABRANIH TEŠKIH METALA U UZORCIMA VINA

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UVOD I CILJ

Teški metali su hemijski elementi čija je relativna gustoća veća od 5 g/cm^3. Dijele se na esencijalne (Cu, Fe, Mn, Zn, Mo, Ni, Cr) i neesencijalne (Cd, Pb, Hg, As, Sn).
Primarni cilj ovog rada bio je odrediti sadržaj odabranih teških metala u uzorcima vina porijeklom sa područja Hrvatske te Bosne i Hercegovine, utvrditi nivo ekspozicije toksičnim metalima putem konzumacije vina i procjeniti potencijalni rizik za zdravlje kod lokalnih proizvođača vina.

METODE

Priprema uzoraka vina (n=57 i to 21 uzorak bijelog, 31 uzorak crvenog i 5 uzoraka rozog vina) je urađena standardiziranom metodom spaljivanja mikrovalnom digestijom *(BAS EN ISO 13804:2015)*. Sadržaj teških metala (Fe, Ni, Cu, As, Pb i Cd) je analiziran na atomskom apsorpcionom spektometru, standardizovanom metodom određivanja sadržaja teških metala u prehrambenim proizvodima *(BAS EN ISO14084:2003)*. Stepen konzumacije vina je procijenjen na osnovu ankete (n=44) dizajnirane za potrebe ovog istraživanja, a provedene među proizvođačima vina tokom augusta 2019.

REZULTATI

Pronađeni sadržaj željeza izražen u mg/L se kretao u rasponima 6.2198-10,1212, 10.9887-17.0312 i 8.0954-12.3210; nikla 0.0234-0.0560, 0.0132-0.0803 i 0.0231-0.0433; bakra 0.0675-0.1213, 0.1063-0.2709 i 0.1002-0.1109; arsena 0.0040-0.0109, 0.0034-0.021 i 0.0054-0.0121; olova 0.0034-0.0121, 0.0045-0.032 i 0.0056-0.0109; kadmijuma 0.0021-0.0197, 0.0022-0.0265 i 0.0088-0.0210 za uzorke bijelog,crnog i rozog vina respektivno. Izračunata medijana i 95-ta percentila stepena konzumacije vina među ispitivanom populacijom iznosila je 50.00 i 1000.00 mL/dan, respektivno. Rezultati procjene izloženosti analiziranim metalima putem konzumacije vina upućuju na zanemarive rizike za zdravlje u slučaju niskih do prosječnih stopa konzumacije wine, ali i namoguće neprihvatljive nivoe rizika kod visokih konzumenata vina.

ZAKLJUČCI

Sadržaj teških metala u analiziranim uzorcima vina je ispod limita postavljenih u važećim pravilnicima u BiH i Europskoj uniji o njihovim maksimalno dopuštenim količinama. Ipak, izračunate vrijednosti za indeks hazarda za pojedine scenarije ekspozicije ukazuju na moguće neprihvatljive nivoe rizika za zdravlje.

KLJUČNE RIJEČI: vino, teški metali, rizik za zdravlje

DETERMINATION OF SELECTED HEAVY METALS IN WINE SAMPLES

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INTRODUCTION AND OBJECTIVE

Heavy metals are chemical elements whose relative density exceedes 5g/cm^3. They are divided between esencial (Cu, Fe, Mn, Zn, Mo, Ni, Cr) and nonesencial (Cd, Pb, Hg, As, Sn).

The primary focus of this paper was to determine the contents of chosen heavy metals in wine samples taken from different vinaries in Croatia and Bosnia and Hercegovina, determine the levels of exposure to toxic metals by consuming wine and determine the potencial health risks asociated with local wine breweries.

METHODS

Wine sample preparation (n=57, containing 21 samples of white wine, 31 samples of red wine and 5 samples of rose) was done by the standard method known as burning microwave digestion (*BAS EN ISO 13804:2015)*. The contets of heavy metals (Fe, Ni, Cu, As, Pb, Cd) is analyzed on an atomic apsorption spectrometer, using a standardized method of determining the contents of heavy metals in food products (*BAS EN ISO 14084:2003*). The amount of wine consumption was determined based on a poll (n=44), specially designed for purposes of this study and conducted between different wine breweryes during August 2019.

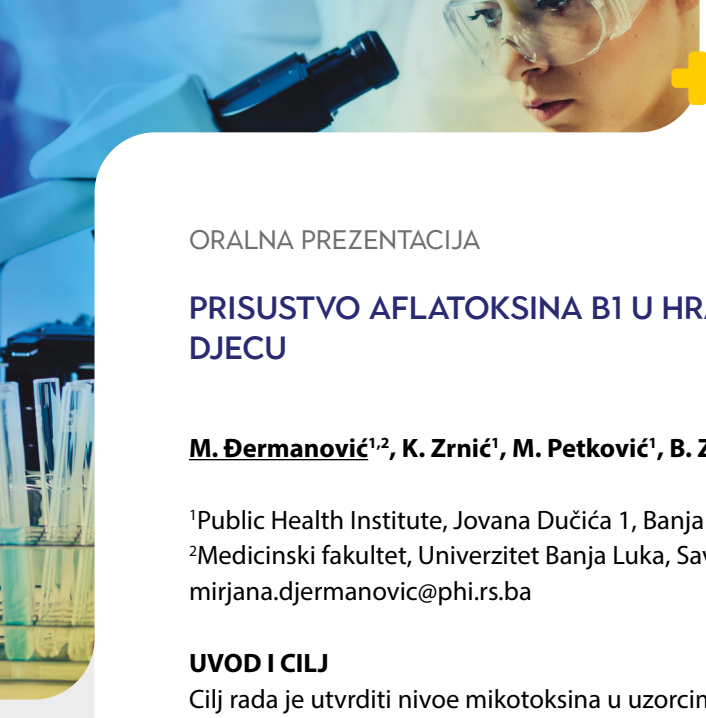
RESULTS

The contents of iron found expressed in mg/L ranged between 6.2198-10,1212, 10.9887-17.0312 and 8.0954-12.3210; Nickel 0.0234-0.0560, 0.0132-0.0803 and 0.0231-0.0433; Copper 0.0675-0.1213, 0.1063-0.2709 and 0.1002-0.1109; Arsen 0.0040-0.0109, 0.0034-0.021 and 0.0054-0.0121; Lead 0.0034-0.0121, 0.0045-0.032 and 0.0056-0.0109; Cadmium 0.0021-0.0197, 0.0022-0.0265 and 0.0088-0.0210 for different samples of white wine, red wine and rose respectively. The calculated median and 95th percentile of wine consumption in the test group was 50.00 and 1000.00 mL/day respectively. The results of exposure to analyzed metals by wine consumption don't seem to point out any or very low health risks in the case of low/average wine consumption, but also show some form of health risk in the case of above average/high levels of wine consumption.

CONCLUSIONS

The contens of heavy metals in analyzed samples of wine are below the limits set by BiH and European Union laws and standards regarding maximum dosages. Still, the calculated values for hazard index for certain scenarios of exposition show possible health risks that are unacceptable.

KEY WORDS: wine, heavy metals, health risks



ORALNA PREZENTACIJA

PRISUSTVO AFLATOKSINA B1 U HRANI NA BAZI ŽITARICA ZA DOJENČAD I MALU DJECU

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UVOD I CILJ

Cilj rada je utvrditi nivoe mikotoksina u uzorcima hrane na bazi žitarica za dojenčad i malu djecu. Plijesni roda Aspergillus najčešći su uzročnici kvarenja hrane, a u nepovoljnim uslovima mogu proizvesti mikotoksine kao toksične sekundarne metabolite. Aflatoksini su grupa mikotoksina koji često onečišćuju različite žitarice. Međunarodna agencija za istraživanje raka (IARC) svrstava aflatoksine u humane karcinogene skupine 1A, a sa stajališta zdravstvene ispravnosti, jedan od najvažnijih mikotoksina je aflatoksin B1. Zbog snažnog karcinogenog, teratogenog i mutagenog djelovanja, čiji su efekti kod ljudi u zavisnosti o nivou i trajanju izlaganja, prisutnost aflatoksina B1 u hrani potrebno je potpuno spriječiti ili zadržati na najnižem mogućem nivou.

METODE

Metoda određivanja aflatoksina uključivala je tečnu hromatografiju visoke djelotvornosti (HPLC; eng. High Performance Liquid Chromatography). HPLC metoda sa fluorescentnim detektorom se odlikuje dobrom osjetljivošću, selektivnošću i ponovljivošću metode, mogućnošću automatizacije (autosempler), kao i kratkim vremenom trajanja analiza. Analizirana su ukupno 52 uzorka.

REZULTATI

Rezultati u 51 analiziranom uzorku su bili ispod granice detekcije (LOD) instrumenta 0,1µg/kg ±20%. Što je u skladu sa važećom zakonskom regulativom u ovoj oblasti. Jedan uzorak je imao vrijednosti koje su bile iznad maksimalno dozvoljenih vrijednosti za ovu grupu proizvoda.

ZAKLJUČCI

Kako prisutnost aflatoksina može biti opasna po zdravlje ljudi, u cilju sprječavanja štetnih efekata, stalna kontrola u hrani je od velikog značaja širom svijeta. U cilju prisustva zdravstveno ispravne hrane potrebna je kontinuirana sistemska kontrola prisustva aflatoksina na reprezentativnom broju uzoraka hrane.

LITERATURA

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KLJUČNE RIJEČI: aflatoksin B1, HPLC, hrana, dojenčad i mala djeca

PRESENCE OF AFLATOXIN B1 IN FOODS BASED ON CEREALS FOR INFANTS AND YOUNG CHILDREN

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INTRODUCTION AND OBJECTIVE

The aim of this study is to determine mycotoxin levels in cereal-based food samples for infants and young children. Molds of the genus Aspergillus are the most common causes of food spoilage and, under adverse conditions, can produce mycotoxins as toxic secondary metabolites. Aflatoxins are a group of mycotoxins that often contaminate a variety of cereals. The International Agency for Research on Cancer (IARC) classifies aflatoxins in human carcinogenic group 1A, and from a health perspective, aflatoxin B1 is one of the most important mycotoxins. Due to the potent carcinogenic, teratogenic and mutagenic effects, which in humans are dependent on the level and duration of exposure, the presence of aflatoxin B1 in food should be completely prevented or kept to the lowest possible level.

METHODS

Method for the determination of aflatoxins included high performance liquid chromatography (HPLC; eng. High Performance Liquid Chromatography). The HPLC method with fluorescence detector is characterized by good sensitivity, selectivity and repeatability of the method, the possibility of automation (autosampler), as well as the short duration of the analyzes. A total of 52 samples were analyzed.

RESULTS

The results of the analyzed sample 51 were below the limit of detection (LOD) of the instrument 0,1µg / kg ± 20%, which is in accordance with current legislation in this field. One sample had values that were above the maximum allowable values for this group of products.

CONCLUSIONS

As the presence of aflatoxins can be hazardous to human health, in order to prevent adverse effects, constant control in food is of great importance worldwide. Continuous systematic control of the presence of aflatoxin on a representative number of food samples is required for the presence of healthy food.

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KEYWORDS: aflatoxin B1, HPLC, food, infants and young children

ORALNA PREZENTACIJA

PREHRAMBENE NAVIKE I TJELESNA AKTIVNOST SREDNJOŠKOLACA SREDNJOBOSANSKOG KANTONA

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UVOD I CILJ

Prehrambene navike i tjelesna aktivnost velikog procenta odraslog stanovništva u FBiH su nezadovoljavajuće [1], a udio gojaznih u odrasloj kao i dječijoj populaciji je dosta visok [1,2]. Prehrana i tjelesna aktivnost krucijalno su značajni preventabilni faktori za hronične nezarazne bolesti. U nekim sredinama se kroz ljekarničku praksu nude dodatne usluge iz domena promocije zdravlja, koje uključuju i savjetovanje o zdravoj tjelesnoj težini, prehrani i životnom stilu. Cilj ovog rada je bio ispitati status uhranjenosti, prehrambene navike i nivo tjelesne aktivnosti kod srednjoškolaca Srednjobosanskog kantona te procijeniti opravdanost uvođenja dodatnih usluga savjetovanja u ljekarnama.

METODE

Podaci su prikupljeni primjenom posebno kreiranog upitnika. Anonimno anketiranje provedeno je u srednjim školama u Kiseljaku, Fojnici i Kreševu u lipnju 2019. Prehrambene navike su procijenjene na osnovu odgovora na pitanja o uobičajenoj konzumaciji namirnica iz pet grupa i dnevnim obrocima te pitanja o uobičajenoj konzumaciji hrane za koju je preporučeno ograničiti unos. Rezultati su prikazani kao ukupan skor pravilne prehrane (skala od 0-14).

REZULTATI

Među ispitanicima (n=693) je bilo 0,9% pothranjenih, 82,2% normalno uhranjenih, 11,9% preuhranjenih i 2,5% gojaznih (podaci nepotpuni kod 2,6% ispitanika). Ukupan skor obrasca prehrane generalno je bio loš (<9) kod nešto više od 85% ispitanika. Istovremeno, oko 25% ispitanika smatra da se zdravo hrani. Preporučeni nivo tjelesne aktivnosti najmanje 4 dana tjedno evidentiran je kod 71,8%, a više 3 sata provedena pred ekranom dnevno kod 86,2% ispitanika. Prethodne konsultacije sa zdravstvenim radnicima prijavilo je 22,7% ispitanika, interes za savjetovanjem 46,5%, a spremnost na promjenu navika 74,7% ispitanika.

ZAKLJUČCI

Iako većina ispitanika ima normalan status uhranjenosti, prehrambene navike su loše kod više od 85% ispitanika. Evidentirana je potreba za dodatnim aktivnostima usmjerenim na poboljšanje obrasca prehrane i smanjenje vremena provedenog pred ekranom, ali i spremnost i interes ispitanika za stručno savjetovanje u ovom domenu. Rezultati sugerišu opravdanost testiranja nove usluge savjetovanja kroz ljekarne.

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KLJUČNE RIJEČI: status uhranjenosti, prehrambene navike, adolescenti, savjetovanje, procjena potreba

DIETARY HABITS AND PHYSICAL ACTIVITY AMONG HIGHSCHOOL STUDENTS IN CENTRAL BOSNIA CANTON

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INTRODUCTION AND AIMS

Dietary habits and physical activity was found to be inadequate in high percent of adult population in FBiH [1], and prevalence of overweight and obesity is high in both adults and children [1,2]. Poor diet and sedentary lifestyle are essential preventable risk factors for noncommunicable chronic diseases. In some regions advanced health promotion services (including dietary and lifestyle counseling and weight management) are offered in pharmacies. The aims of this work were to assess nutrition status, dietary habits and physical activity level among high school students in Central Bosnia Canton as well as assessment of justification of dietary and lifestyle counseling service in local pharmacies.

METHODS

Data were collected by specially designed anonymous, self-administered questionnaire during June 2019. Dietary habits were assessed based on habitual intake of food from the main food groups, number of meals per day and frequency of consumption of food that should be limited. Results are expressed as healthy diet score (scale 0-14).

RESULTS

In the total sample (n=693) malnutrition was recorded in 0,9%, normal nutritional status in 82,2%, overweight in 11,9% and obesity in 2,5% of participants (incomplete data in 2,6% participants). The total healthy diet score was low (<9) in about 85% participants. Interestingly, about 25% of participants believed that their dietary habits were good. The recommended level of physical activity at least 4 days in a week was reported by 71,8%, but the screen time of more than 3 hours per day was reported by 86,2% of the participants. Previous dietary counseling with health professionals was reported by 22,7%, while interest in such counseling was reported by 46,5%, and readiness for behavioral changes was expressed by 74,7% of the participants.

CONCLUSIONS

Although the majority of participants were in normal BMI range, poor dietary habits were found in more than 85% of the participants. The results show the need for additional activities for improvement of dietary habits and reduction in screen time, but also participants' willingness to change behavior and interest for professional counseling service. Field testing of advanced counseling service in pharmacies is justified.

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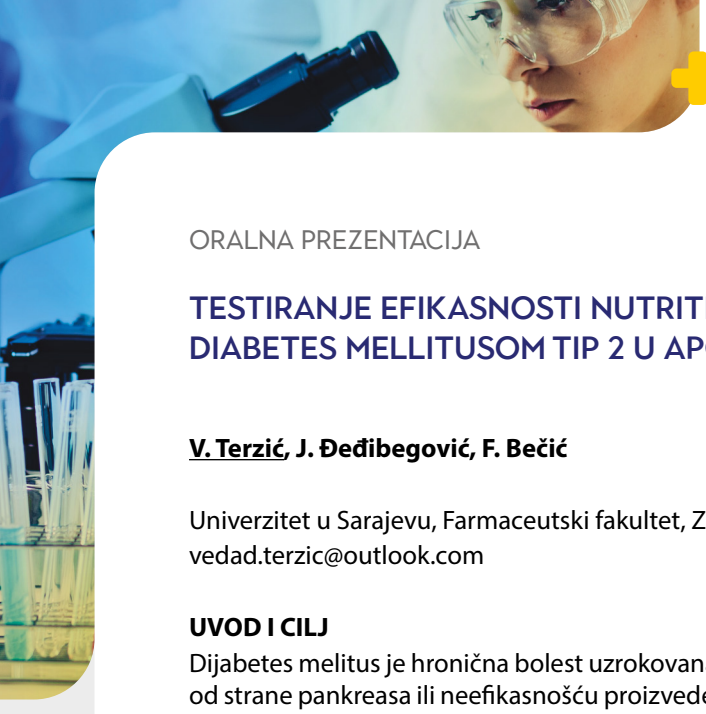
KEY WORDS: nutrition status, dietary habits, adolescents, dietary counseling, needs assessment



ORALNA PREZENTACIJA

TESTIRANJE EFIKASNOSTI NUTRITIVNOG SAVJETOVANJA PACIJENATA S DIABETES MELLITUSOM TIP 2 U APOTECI

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UVOD I CILJ

Dijabetes melitus je hronična bolest uzrokovana nasljeđenim i / ili stečenim nedostatkom proizvodnje inzulina od strane pankreasa ili neefikasnošću proizvedenog inzulina. (1) Prema podacima koje prikazuje IDF (International Diabetes Federation – Internacionalna Federacija za dijabetes) broj osoba sa dijabetes melitusom u Evropi će sa već postojećih 66 miliona dijagnosticiranih slučajeva dijabetes melitusa porasti na 81 milion slučajeva do 2045. godine. (2) Pravilna prehrana je jedan od tri glavna elemente kontrole ovog oboljenja i odgađanja komplikacija koje mogu nastati kao posljedica ove bolesti. Cilj provedene studije je bio ispitati efikasnost nutricionističkog savjetovanja pacijenta od strane farmaceuta u apoteci sa ciljem optimizacije kontrole dijabetesa melitusa tip 2.

METODE

Regrutovano je 10 ispitanika u apoteci čije je znanje prije edukacija evaluirano upitnikom na inicijalnom sastanku. Nakon toga su ispitanici dobili edukacije o prehrani u dijabetes melitusu u periodu od 2 mjeseca u apoteci. Progres koji su pacijenti napravili tokom ovog dvomjesečnog perioda ispitan je upitnikom na završnom sastanku.

REZULTATI

Kod ispitanika zabilježen je nešto veći napredak unapređenje obrasca prehrane nego u usvajanje teoretskog znanja. Imajući u vidu da je edukacija prosječno po pacijentu trajala samo jedan sat, postignute efekte možemo ocijeniti kao izuzetne.

ZAKLJUČCI

Rezultati ove studije mogu poslužiti kao osnova za formulisanje usluge nutritivnog savjetovanja za pacijente s dijabetes melitusom kroz apoteke u našoj sredini.

LITERATURA

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KLJUČNE RIJEČI: Diabetes mellitus, nutricija, savjetovanje, apoteka, javna zdravstvena ustanova

TESTING EFFICIENCY OF NUTRITIONAL COUNSELING OF PATIENTS WITH DIABETES MELLITUS TYPE 2 IN PHARMACY

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INTRODUCTION AND OBJECTIVE

Diabetes mellitus is a chronic disease caused by an inherited and / or acquired deficiency of insulin production by the pancreas or by the inefficiency of insulin produced. (1)

According to data provided by the International Diabetes Federation (IDF), the number of people with diabetes mellitus in Europe will increase from 66 million already diagnosed cases of diabetes mellitus to 81 million by 2045. (2) Proper nutrition is one of the three main elements of controlling this disease and delaying the complications that can result from this disease. The aim of the study was to examine the efficacy of nutrition counseling of patients by pharmacist in a pharmacy in order to optimize control of type 2 diabetes mellitus.

METHODS

10 subjects were recruited from a pharmacy whose pre-education knowledge was evaluated by a questionnaire at the initial meeting. Subsequently, the subjects received nutrition education in diabetes mellitus for a period of 2 months at a pharmacy.

The progress patients made during this two-month period was examined by a questionnaire at the final meeting.

RESULTS

There was a slight improvement in the improvement of the dietary pattern in the subjects than in the acquisition of theoretical knowledge. Considering that the average education per patient lasted only one hour, the effects achieved can be considered exceptional.

CONCLUSIONS

The results of this study may serve as a basis for formulating a nutritional counseling service for patients with diabetes mellitus through pharmacies in our community.

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KEY WORDS: Diabetes mellitus, nutrition, counseling, pharmacy, public health pharmacy

POSTER

SADRŽAJ TEŠKIH METALA U MORSKIM PLODOVIMA NA BIH TRŽIŠTU

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UVOD I CILJ

Zbog svojih izuzetnih nutritivnih svojstava riba se smatra značajnim dijelom zdrave prehrane. Međutim, riba i morski plodovi su i značajan izvor dijetarne ekspozicije teškim metalima. Toksični efekti teških metala uključuju: oštećenje funkcije bubrega i jetre, smanjenje kognitivne i reproduktivne funkcije, hipertenziju, neurološke i teratogene efekte i karcinome. Naša ranija istraživanja su pokazala sadržaj teških metala u pojedinim uzorcima riba iz Neretve veći od maksimalno dozvoljene koncentracije (MDK), a u većem broju uzoraka u koncentracijama koje mogu predstavljati zdravstveni rizik u učestalijoj konzumaciji.
Cilj istraživanja je odrediti sadržaj toksičnih metala (Pb, Cd, Hg) u jestivom dijelu ribe i morskih plodova na BiH tržištu, te izvesti procjenu rizika za konzumente.

METODE

Analiza je izvedena u akreditiranom laboratoriju za analizu hrane Veterinarskog fakulteta Univerziteta u Sarajevu. Uzorci su pripremljeni u skladu sa standardnom metodom BAS EN 13 804 i BAS EN 13 805 i analizirani GF-AAS tehnikom primjenom standardne metode BAS EN ISO 14084 za kadmij i olovo, dok je sadržaj žive određen validiranom in-house metodom. Kontrola kvaliteta postupka izvedena je primjenom ERM® (*European Reference Materials*) certificiranog referentnog materijala (tkivo školjke za analizu elemenata).

REZULTATI

U analiziranim uzorcima (oslić, tuna, skuša, lignja, dagnje, gamberi; n=37) sadržaj olova kadmija i žive je bio u granicama od nedetektabilnog (< 0,001 mg/kg) – 0,278 mg/kg, 0,002 – 0,918 mg/kg i 0,018 - 0,624 mg/kg. Sadržaj veći od maksimalno dozvoljenog nađen je jedino za živu u jednom uzorku (skuša), dok je u svim uzorcima lignje nađen značajno veći sadržaj kadmija nego u ostalim uzorcima.

ZAKLJUČCI

Prema nađenom sadržaju kadmija konzumacijom 200-400 g lignje sedmično odrasla osoba (70 kg) bi prekoračila tolerantni sedmični unos za kadmij koji preporučuje Evropske agencija za sigurnost hrane (EFSA) (2,5 µg/kg tjelesne mase), ne uzimajući u obzir ostale izvore ekspozicije. Rizik za populaciju će se moći egzaktnije procijeniti u kombinaciji s rezultatima totalne dijetarne studije koju trenutno provodi Agencija za sigurnost hrane BiH.

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[3] EFSA Panel on Contaminants in the Food Chain. Scientific Opinion: Statement on tolerable weekly intake for cadmium. EFSA J. 2011. Available from: www.efsa.europa.eu/efsajournal.

KLJUČNE RIJEČI: riba, morski plodovi, živa, kadmij, olovo

Izvori finansiranja: *Ovaj rad je finansiran od Federalnog ministarstva obrazovanja i nauke, FBiH kroz grant za naučnoistraživački projekat.*

HEAVY METAL CONTENT IN SEAFOOD FROM BIH MARKET

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INTRODUCTION AND OBJECTIVE

Due to its exceptional nutritional properties, fish is considered a significant part of a healthy diet. However, fish and other seafood are also a significant source of dietary exposure to heavy metals. The toxic effects of heavy metals include: impaired renal and hepatic function, decreased cognitive and reproductive function, hypertension, neurological and teratogenic effects, and cancers. Our previous study has shown that the content of heavy metals in certain samples of Neretva fish exceeds that of MRL (maximum residue level), and in a number of samples content that suggests potential health risk in high-end consumers.

The aim of this study was to determine the content of toxic metals (Pb, Cd, Hg) in the edible part various seafood in the BiH market and to assess potential risk for consumers.

METHODS

The analysis was performed in an accredited food control laboratory at the Faculty of Veterinary Medicine, University of Sarajevo. Samples were prepared according to the standard BAS EN 13 804 and BAS EN 13 805 methods and analyzed by the GF-AAS technique using the standard BAS EN ISO 14084 method for cadmium and lead, while mercury content was determined by a validated in-house method. Process quality control was performed using an ERM® (European Reference Materials) certified reference material (mussel tissue for element analysis).

RESULTS

In the analyzed samples (hake, tuna, mackerel, squid, mussel, shrimp; n = 37) the content of lead, cadmium and mercury was in the range of undetectable (<0.001 mg/kg) to 0.278 mg/kg, 0.002 - 0.918 mg/kg and 0.018 - 0.624 mg/kg. kg, respectively. Level above the maximum residue level was found only for mercury in one sample (mackerel), while cadmium content in all squid samples was significantly higher than in the other analyzed samples.

CONCLUSIONS

Given the cadmium content found, an adult person (70 kg bw) would exceed the tolerable weekly intake recommended by European Food Safety Authority -EFSA (2.5 µg/kg body weight) only by consuming 200-400 g of squid per week, without taking into account other sources of exposure. The risk to the population will be more accurately assessed in combination with the results of the total dietary study currently conducted by the BiH Food Safety Agency.

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KEY WORDS: fish, seafood, mercury, cadmium, lead

Funding statement: *This work was funded by the Federal Ministry of Education and Science, FBiH.*

POSTER

SPEKTROFOTOMETRIJSKO ODREĐIVANJE UKUPNIH UGLJIKOHIDRATA U PRIRODNIM SOKOVIMA

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UVOD I CILJ

Ugljikohidrati se nalaze se u velikom broju namirnica, a uobičajeni su sastojci i različitih sokova. Procjena kvalitete i autentičnosti prirodnih sokova važno je primijenjeno istraživačko područje s relevantnim uticajem na industriju, nauku o hrani i zaštitu potrošača. Brze i ekonomične metode kvantifikacije ugljikohidrata u prirodnim sokovima su od velike važnosti, jer brojne kompanije, proizvođači ili trgovci traže ekonomsku dobit koristeći prirodne sokove lošije kvalitete za dobivanje tržišnih prednosti u odnosu na poštene konkurente, koristeći jeftinije sastojke (umjetne zaslađivače, šećer i sirupe) [1, 2]. Stoga, cilj ovog rada je odrediti količinu ukupnih ugljikohidrata u 100 % prirodnim sokovima.

METODE

Ukupni ugljikohidrati određeni su u deset prirodnih sokova (drenjak, breskva, višnja, jabuka, narandža i višnja) različitih proizvođača komercijalno dostupnih na tržištu BiH. Uzorci sokova su filtrirani, potom razblaženi sa destilovanom vodom u omjeru 1:1000. U razblaženi uzorak dodana je otopina Anthrona (2 mg mL-1), te se smjesa zagrijavala u vodenom kupatilu, pri čemu se razvila zelena boja čiji intenzitet zavisi koncentraciji topivih ugljikohidrata. Zatim se provodi hlađenje na ledu i spektrofotometrijski mjeri apsorbancija pri 630 nm.

REZULTATI

Dobivene koncentracije ukupnih ugljikohidrata u analiziranim sokovima bile su u rasponu 3.39 – 14.62 g mL^{-1}, a u deklarisanim 8.70-14.00 g mL^{-1}. Najveća koncentracija zabilježena je u soku od breskve, a najmanja u soku od narandže, dok je kod deklarisanih najveća kod višnje, a najmanja kod narandže. Rezultati analize pokazali su da u devet uzoraka, sadržaj ukupnih ugljikohidrata ima manje vrijednosti u odnosu na deklarisane, dok je u jednom uzorku veći.

ZAKLJUČCI

Spektrofotometrijsko određivanje ukupnih ugljikohidrata upotrebom Anthronovog reagensa pokazalo se kao brza i ekonomična metoda u odnosu na savremenije metode poput refraktometrije i HPLC. S obzirom na rezultate analize i činjenicu da eksperimentalno dobijeni rezultati sadržaja ukupnih ugljikohidrata nisu u skladu sa deklarisanim, trebalo bi paziti na izbor komercijalno dostupnih prirodnih sokova.

LITERATURA:

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KLJUČNE RIJEČI: ugljikohidrati, prirodni sokovi, spektrofotometrija, Antronov reagens.

SPECTROPHOTOMETRIC DETERMINATION OF TOTAL CARBOHYDRATES IN NATURAL JUICES

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INTRODUCTION AND OBJECTIVE

Carbohydrates are a component of many foods and are the common constituents of various juices. Assessment of natural fruit juices quality and authenticity is an important applied research area with relevant impact on the industry, food science, and consumer protection. Rapid and cost-effective methods of quantification of carbohydrates in natural juices are of high importance, since many companies, manufacturers or traders seeking economic gain using natural juices lower quality to gain a market advantage over honest competitors using cheaper ingredients (artificial sweeteners, sugar, and syrups) [1, 2]. Therefore, the aim of the present study was to determine of total carbohydrates in 100 % natural juices.

METHODS

Total carbohydrates are determined in ten natural juices (cornel berries, peach, cherry, apple, orange, and cherry) from several manufacturers commercially available in the market of B&H. The juice samples were filtered and diluted with distilled water at a ratio of 1:1000. To the diluted sample was added Anthron solution (2 mg mL^{-1}). The mixture was heated in a water bath, developing a green color whose intensity was dependent on the concentration of soluble carbohydrates. Then it is cooled on ice and the absorbance measured at 630 nm by spectrophotometry.

RESULTS

The obtained concentrations of total carbohydrates in the analyzed juices were in the range 3.39 - 14.62 g m^{L-1} and in the declared 8.70-14.00 g mL-1. The highest concentration was been in peach juice and the lowest in orange juice, while the highest concentration was found in cherry and the lowest in orange. Analysis of the results shown that in nine samples, the total carbohydrate content has lower values than declared, while in one sample it was higher.

CONCLUSIONS

Spectrophotometric determination of total carbohydrates by using Anthron reagents shown to be a quick and economical method concerning more sophisticated methods, such as HPLC, and refractometry. Considering the results of the analysis and the fact that the experimentally obtained results of the content of total carbohydrates are not by the declared ones, the choice of commercially available natural juices should be considered.

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KEY WORDS: carbohydrates, natural juices, spectrophotometry, Anthron reagent.

POSTER

MIKROBIOLOŠKA ISPRAVNOST DJEČIJE HRANE U REPUBLICI SRPSKOJ U 2017. GODINI

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UVOD I CILJ

Mikrobiološka ispravnost predstavlja izuzetno značajan parametar zdravstvene ispravnosti. Mikrobiološka kontaminacija hrane može da bude uzrok veoma ozbiljnih zdravstvenih komplikacija koje nastaju kao posljedica bolesti izazvanih unosom kontaminirane hrane. Pravilnikom o mikrobiološkim kriterijumima za hranu utvrđeni su mikrobiološki kriterijumi za određene mikroorganizme u hrani koji moraju da budu zadovoljeni u cilju proizvodnje i distribucije zdravstveno ispravne hrane krajnjem potrošaču. *Cilj rada* je dati pregled mikrobiološkog kvaliteta dječije hrane koja je ispitana u 2017. godini u Republici Srpskoj.

METODE

Podaci o mikrobiološkoj ispravnosti dječije hrane su preuzeti iz godišnjeg izvještaja o zdravstvenom stanju stanovništva Republike Srpske koji izrađuje Institut za javno zdravstvo Republike Srpske.

REZULTATI

U 2017. godini na mikrobiološku ispravnost ispitano je 179 uzoraka, pri čemu je 93,3% uzoraka je pregledano prilikom uvoza i 6,7 % iz prometa. Od toga 5 uzoraka je bio mikrobiološki neispravno (2,8%). Što se tiče rezultata pregleda uzoraka na pojedine mikroorganizme, u najviše neispravnih uzoraka su izolovane *Enterobacteriaceae sp.* (5), zatim kvasac i plijesni (5).

ZAKLJUČCI

S obzirom na pronađenu zdravstvenu neispravnost namirnica sa aspekta mikrobioloških kriterijuma, potrebno je nastaviti i pojačati kontinuiranu kontrolu zdravstvene ispravnosti namirnica u Republici Srpskoj, naročito dječije hrane koja je namijenjena osjetljivoj populaciji dojenčadi i male djece i drugim vulnerabilnim kategorijama stanovništva.

LITERATURA

[1] Bilten- Zdravstveno stanje stanovništva Republike Srpske, Institut za javno zdravstvo Republike Srpske

KLJUČNE RIJEČI: hrana, djeca, zdravstvena ispravnost, mikroorganizmi

MICROBIOLOGICAL QUALITY FOOD INTENDED FOR INFANTS AND SMALL CHILDREN IN THE REPUBLIC OF SRPSKA IN 2017

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INTRODUCTION AND OBJECTIVE

The microbiological food quality is an extremely important parameter for foodstuffs. Microbiological food contamination can be the cause of very serious health complications caused by the ingestion of contaminated food. The Ordinance on microbiological criteria for food has established microbiological criteria for certain microorganisms in food that must be met in order to produce and distribute safe food to the consumer. The aim of this paper is to give an overview of the microbiological quality of food that was tested in 2017 in the Republic of Srpska.

METHODS

The data on microbiological food intended for infants and small children safety are taken from the annual report on the health condition of the population of the Republic of Srpska, prepared by the Public Health Institute of the Republic of Srpska.

RESULTS

In 2017, 179 samples of food intended for infants and small children were tested for microbiological correctness (93.3% from import, 6.7% from the market). Out of that, 5 samples were microbiologically defective (2,8%). As for the results of the examination of the samples on individual microorganisms, *Enterobacteriaceae sp.* were detected in 5 samples, then yeast and mold in 5.

CONCLUSIONS

It is necessary to continue and strengthen the continuous control of the food safety in the Republic of Srpska, especially food intended for the sensitive population of infants and young children and other vulnerable population.

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KEY WORDS: food, children, health, microorganisms

POSTER

USKLAĐENOST SADRŽAJA OMEGA 3 MASNIH KISELINA SA DEKLRISANIM VRIJEDNOSTIMA KOD DODATAKA ISHRANI

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UVOD I CILJ

Istraživanjem uticaja omega-3 masnih kiselina na zdravlje ljudi, utvrđen je niz dobrobiti pa se u današnje vrijeme brzog načina života pojavila potreba za proizvodnjom lako dostupnog izvora omega-3 masnih kiselina. Dugolančane polinezasićene masne kiseline (EPA/DHA) u ljudskoj ishrani uglavnom se dobijaju ishranom koja sadrži „masne" ribe ili uzimajući dodatke ishrani koji sadrže navedene kiseline.

METODE

Određivanje količine zasićenih i nezasićenih masnih kiselina je rađeno postupkom poznatim kao FAME (eng. Fatty acid methyl ester analasys). Masti se određuju pomoću ekstrakcije hladnim rastvaračem kao što je DCM (dihlormetan). Ekstrakti se osuše i derivatizuju kako bi se formirali metil esteri masnih kiselina, korištenjem reagensa kao što je bor triflorid. Razdvajanje masnih kiselina i njihovo određivanje urađeno je metodom gasne hromatografije. Kao gas nosač u provedenom eksperimentu korišten je helijum, protok je bio 25 mL/min. Korištena kolona je Rastek Famewax (30 m, 0.32 mm, 0.25 µm). Split je iznosio 50:1, detektor: plameno jonizacijski detektor, dok je vrijeme analize bilo 50 minuta.

REZULTATI

Rezultati su pokazali da je određeni sadržaj omega 3 masnih kiselina bio u saglasnosti sa deklarisanim sadržajem kod 12 uzoraka (85.7 %). Negativno odstupanje određenog sadržaja od deklarisane vrijednosti utvrđeno je kod 2 uzorka.

ZAKLJUČCI

Brz tempo života, stres, neredovna i nepravilna ishrana i nedovoljna fizička aktivnost su samo neki od faktora koji uslovljavaju sve veću upotrebu dodataka ishrani u cilju postizanja i održavanja dobrog zdravstvenog stanja, prevencije bolesti, kao i povećanja snage i izdržljivosti. Osnovni uslov da bi se dodaci ishrani plasirali na tržište jeste da budu bezbjedni, kvalitetni i efikasni. Da bi se osnovni uslovi ispunili potrebno je poštovanje uslova koje daju zakonski propisi, sa precizno definisanim uslovima kvaliteta i bezbjednosti.

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KLJUČNE RIJEČI: omega-3 masne kiseline, dodaci ishrani, sadržaj, gasna hromatografija

COMPLIANCE OF THE OMEGA 3 FATTY ACIDS WITH DECLARED VALUES IN THE FOOD SUPPLEMENT

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INTRODUCTION AND OBJECTIVE

Research into the impact of omega-3 fatty acids on human health has identified a lot of benefits, so in the fast-paced lifestyle today there is a need to produce an easily accessible source of omega-3 fatty acids. Long-c-hain polyunsaturated fatty acids (EPA / DHA) in the human diet are generally obtained from a diet containing "fat" fish or by taking food supplements containing these acids.

METHODS

The determination of saturated and unsaturated fatty acids was performed by a method known as FAME (Fatty acid methyl ester analasys). The fat is extracted from the sample by extraction with a cold solvent such as DCM (dichloromethane). The extracts are dried and derivatized to form fatty acid methyl esters, using reagents such as boron trifloride. The separation of fatty acids and their determination was done by gas chromatography. Helium was used as the carrier gas in the experiment, the flow rate was 25 mL / min. The column used was Rastek Famewax (30 m, 0.32 mm, 0.25 µm). Split was 50: 1, detector: flame ionization detector, while analysis time was 50 minutes.

RESULTS

The results showed that a certain content of omega 3 fatty acids was in agreement with the declared content in 12 samples (85.7%). Negative deviation of certain content from declared value was found in 2 samples.

CONCLUSIONS

Fast pace of life, stress, irregular diet and insufficient physical activity are just some of the factors behind the increasing use of food supplements to achieve and maintain good health, prevent disease, and increase strength and endurance. A prerequisite for a dietary supplement to be marketed is that it is safe, of good quality and effective. In order to meet the basic requirements, it is necessary to observe the conditions given by the legal regulations, with precisely defined conditions of quality and safety.

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KEYWORDS: omega 3 fatty acids, dietary supplement, content, gas chromatography

POSTER

DIJETARNE INTERVENCIJE KOD OBOLJELIH OD ALS-A

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UVOD I CILJ

Amiotrofična lateralna skleroza (ALS) je neurodegenerativna bolest koju karakteriše progresivna mišićna slabost. Manifestuje se znacima poremećaja gornjeg i donjeg motornog neurona. Bolest je progresivna i atrofija postepeno zahvata sve mišiće. Dijagnoza se temelji na kliničkoj slici, elektrodijagnostičkom testiranju i isključenju stanja koja mogu imitirati ALS.

METODE

Ispitati dostupnost hrane za posebne medicinske potrebe oboljelima od ALS u Republici Srpskoj.

REZULTATI

Uvidom u podatke Fonda zdravstvenog osiguranja Republike Srpske, dobijeni su podaci da su od 1.1.2017 godine oboljelima od ALS širom Republike Srpske dostupni preperati iz grupe hrane za posebne medicinske potrebe. Isti se dobijaju preko recepta, na teret osiguranja što njihovim porodicama olakšava brigu oko oboljelog.

ZAKLJUČCI

Optimalan tretman temelji se na liječenju simptoma i održavanju kvaliteta života. U današnje vrijeme, postoji sve veće interesovanje za ulogu ishrane u patogenezi i progresiji amiotrofične lateralne skleroze. Postoji veliki broj mikronutrijenata, makronutrijenata i grupa namirnica koje mogu potencijalno povećati ili smanjiti oksidativni stres koji se smatra jednim od glavnih uzroka nastanka ALS-a.

LITERATURA

[1] Pozitivna lista lijekova Fonda Zdravstvenog osiguranja Republike Srpske

KLJUČNE RIJEČI: hrana, djeca, zdravstvena ispravnost, mikroorganizmi

DIATARY INTERVENTIONS IN ALS PATIENTS

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INTRODUCTION AND OBJECTIVE

Amyotrophic lateral sclerosis (ALS) is neurodegenerative disorder characterized by progressive muscular weakness. It affects both upper and lower motor neurons. The diagnosis of ALS is based on clinical features, electrodiagnostic testing, and exclusion of conditions that can mimic ALS. Optimal treatment is based on symptoms management and preservation of quality of life.

METHODS

To examine the availability of food for special medical needs for patients with ALS in Republika Srpska.

RESULTS

An insight into the data of the Health Insurance Fund of the Republika Srpska reveals that from January 1, 2017, patients with ALS across the Republika of Srpska were able to access food for special medical needs. That specific food obtained through a prescription, at the expense of insurance, which makes it easier for their families to care for the patient.

CONCLUSIONS

Today, there is a growing interest in the role of nutrition in the pathogenesis and progression of amyotrophic lateral sclerosis. There are some micronutrients, macronutrients and groups of food that potentially could increase or decrease oxidative stress, which is one of risk factors for ALS development.

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KEY WORDS: dietary interventions, foods for special medical needs, patients, ALS

POSTER

IDENTIFIKACIJA SLOBODNIH AMINOKISELINA DIVLJIH JESTIVIH GLJIVA: ZALEĐENIH I SUŠENIH

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UVOD I CILJ

Gljive su dobar izvor proteina, odnosno esencijalnih aminokiselina, dijetalnih vlakana, različitih makro i esencijalnih elemenata, te sadrže malu količinu masti i holesterola [1,2].

Cilj ovog rada je odrediti slobodne aminokiseline u odabranim divljim jestivim gljivama koje su konzervirane: sušenjem i zaleđivanjem.

METODA

Slobodne aminokiseline: valin (Val), leucin (Leu), fenilalanin (Phe), triptofan (Trp) i metionin (Met), arginin (Arg), glicin (Gly), tirozin (Tyr), L-alanin (L-Ala) i cistein (Cys) identifikovane su pomoću TLC (tankoslojne hromatografije) u gljivama koje su sušene (univerzalna tunelska peć: 35°C, 6-8h) i zaleđene (-20° C). Analiza tako konzerviranih gljiva urđena je nakon mjesec dana. Analizirani su etanolski ekstrakti gljiva: *Boletus edulis* (vrganj), *Lactarius piperatus* (mliječnica), *Cantharellus cibarius* (lisičarka), *Cantharellus tubaeformiss* (zlatna lisičarka), *Craterellus cornucopioides* (truba) i *Hydnum repandum* (ježavka). Za kvalitativnu analizu korištene su: TLC pločice SIL-G60 10x20cm; Mobilna faza: 2-butanol-glacijalna acetilna kiselina-dejonizirana voda (8:2:2); za vizualizaciju: otopina ninhidrina (0,2%) u 95 % acetonu.

REZULTATI

TLC analizom identifikovane su slobodne aminokiseline kod zaleđenih uzoraka i to kod mliječnice: Arg, Cys, Met, L-Ala, Gly, Phe i Tyr; Vrganja: Arg, Met, Gly, Phe i Tyr: Trube: Arg, Met, L-Ala, Gly, Phe i Tyr; Ježavke: Arg, Met, Gly i Tyr; lisičarke: Arg, Met, Val, Gly i Phe; zlatne lisičarke: Arg, Cys, L-Ala, Val i Gly.

Također, slobodne aminokiseline su identifikovane i kod suhih uzoraka i to kod mliječnice: Arg, L-Ala, Val, Gly i Tyr; Vrganja: Trp, Arg, L-Ala, Val, Leu i Tyr: Trube: Trp, Arg, L-Ala, Val, Leu i Tyr; Ježavke: Arg, L-Ala, Val, Gly i Tyr; lisičarke: Trp, Arg, Leu, Phe i Tyr; zlatne lisičarke: Arg, L-Ala, Val i Tyr.

ZAKLJUČCI

Rezultati pokazuju da način konzerviranja gljiva (sušenje i zamrzavanje) nema veliki uticaj na zastupljenost slobodnih aminokiselina. Na osnovu dobijenih rezultata kao i na osnovu literaturnih podataka može se zaključiti da su odabrane vrste gljiva potencijalni izvori nutraceutika. Svakako je potrebno i neophodno nastaviti dalja istraživanja ovih vrsta gljiva.

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KLJUČNE RIJEČI: divlje jestive gljive, slobodne aminokiseline, TLC-metoda

QUALITATIVE ESTIMATION AMINO ACIDS OF WILD EDIBLE MUSHROOMS: FROZEN AND DRIED

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INTRODUCTION AND OBJECTIVE

Mushrooms are a good source of protein, essential amino acids (AA), dietary fiber, various macro and essential elements, and contain little fat and cholesterol [1,2].

This study aimed to determine the free AA in selected wild edible mushrooms that were preserved: frozen and dried.

METHOD

Free AA: valine (Val), leucine (Leu), phenylalanine (Phe), tryptophan (Trp) and methionine (Met), arginine (Arg), glycine (Gly), tyrosine (Tyr), L-alanine (L-Ala), and cysteine (Cys) were determined by TLC (thin layer chromatography) in mushrooms that were dried (universal tunnel oven, 35°C, 6-8h) and frozen (-20° C). The analysis of that mushrooms thus preserved was made after one month. Ethanol extracts of mushrooms were analyzed: *Boletus edulis*, *Lactarius piperatus*, *Cantharellus cibarius*, *Craterellus cornucopioides*, *Cantharellus tubaeformiss*, and *Hidnum repandum*. For the qualitative analyse, were used: TLC-plates SIL-G60 10x20cm, mobile phase: 2-butanol-glacial acetyl acid-deionized water (8:2:2), and for visualization: ninhydrin solution (0.2%) in 95% acetone.

RESULTS

Free AA were identified by the TLC method in frozen mushrooms, the following, *Lactarius piperatus*: Arg, Cys, Met, L-Ala, Gly, Phe, Tyr; *Boletus edulis*: Arg, Met, Gly, Phe, Tyr; *Craterellus cornucopioides*: Arg, Met, L-Ala, Gly, Phe, Tyr; *Hidnum repandum*: Arg, Met, Gly, Tyr; *Cantharellus cibarius*: Arg, Met, Val, Gly, Phe; *Cantharellus tubaeformiss*: Arg, Cys, L-Ala, Val, Gly.

Also, free AA were identified in dried mushrooms, the following, *Lactarius piperatus*: Arg, L-Ala, Val, Gly, Tyr; *Boletus edulis*: Trp, Arg, L-Ala, Val, Leu, Tyr; *Craterellus cornucopioides*: Trp, Arg, L-Ala, Val, Leu, Tyr; *Hidnum repandum*: Arg, L-Ala, Val, Gly, Tyr; *Cantharellus cibarius*: Trp, Arg, Leu, Phe, Tyr; *Cantharellus tubaeformiss*: Arg, L-Ala, Val, Tyr.

CONCLUSIONS

The results showed that preserved mushrooms, drying or freezing does not have a major effect on the representation of free AA. It can be concluded on the based obtained results and the literature data, that the selected types of mushrooms are potential sources of nutraceuticals. It is certainly necessary to continue further research into these types of mushrooms.

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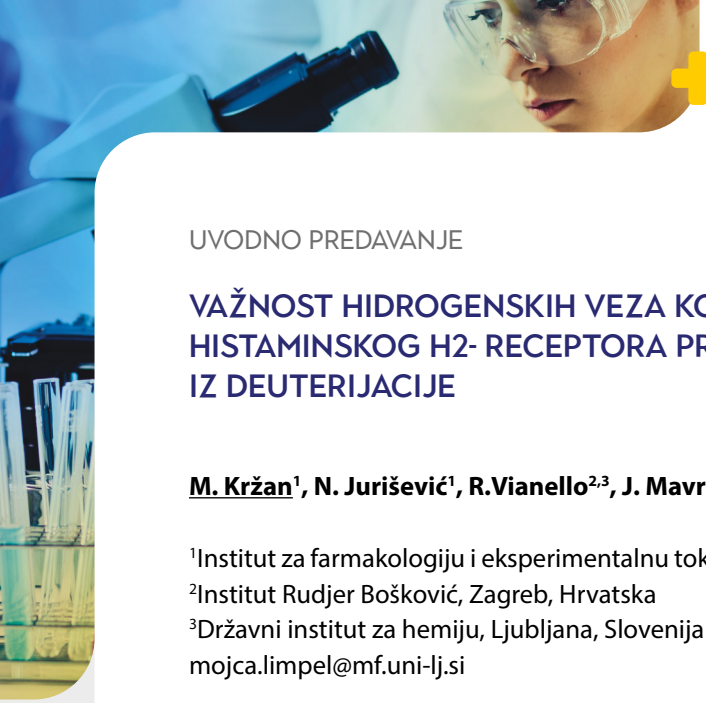
KEYWORDS: edible wild mushrooms, free amino-acids, TLC-method.

KLINIČKA FARMACIJA I FARMAKOLOGIJA



UVODNO PREDAVANJE

VAŽNOST HIDROGENSKIH VEZA KOD VEZIVANJA I FUNKCONALNE OSOBINE HISTAMINSKOG H2- RECEPTORA PRISUTNIH U ASTROCITIMA PACOVA – LEKCIJA IZ DEUTERIJACIJE

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UVOD I CILJ

Histaminski H2 receptor je član porodice receptora G-proteina čija domena vezivanja postoji u manjoj mjeri u okviru lipidnog podsloja. Ključnu ulogu kod vezivanja histamina za histaminski H2 receptor igra formiranje hidrogenskih veza između ostataka aminokiselina u trećoj i petoj transmembrane alfa-zavojnice (Asp^{98}, Asp^{186} i Tyr^{250}) i tri atoma nitrogena histaminske molekule.

METODE

Kako bi se procijenila važnost vodikovih veza u procesu vezivanja liganda za H2 receptor te njegova daljnja funkcija, uporedili smo svojstva vezivanja histaminergičnih liganada za mjesto vezivanja histaminskog H2 receptora na uzgojenim astrocitima novorođenih pacova u kontrolnom i deuteriranom mediju s rezultatima kvantnih hemijskih izračuna. Pored toga, odredili smo produkciju cAMP nakon stimulacije s antagonistom u kontrolnom i u deuteriranom mediju.

REZULTATI

Eksperimenti jasno pokazuju da deuteracija utiče na vezivanje kroz povećanje afiniteta prema histaminu i 4-metilhistaminu te smanjenje afiniteta prema di-metilhistaminu, dok se afinitet ne mijenja za cimetidin i famotidin. Kvantni hemijski izračuni na klaster sistemu estrahiranom iz homologije H2 modela zajedno s implicitnom kvantizacijom kiselih veza N-H i O-H, pokazuje da se ove promjene u vezivanju mogu racionalizirati kroz promijenjenu snagu vezivanja vodika nakon deuteracije poznate kao Ubbelohdeov efekat. Deuteracija je uticala na signalna svojstva glijalnog H2 receptora, ali samo u slučajevima u kojima je korištena milimolarna koncentracija histamina.

ZAKLJUČAK

Supstitucija liganda H/D je relevantna za terapiju u kontekstu (per)deuteriziranih i stoga stabilnijih lijekova za koje se očekuje da uđu u terapijsku praksu u skoroj budućnosti. Nadalje, predstavljeni pristup može doprinijeti razumijevanju aktivacije receptora, dok dugoročni cilj ostaje u siliko-diskriminaciji agonista i antagonista baziranoj na strukturi receptora.

RELEVANCE OF HYDROGEN BONDS IN BINDING AND FUNCTIONAL PROPERTIES OF HISTAMINE H2- RECEPTOR PRESENT IN RAT ASTROCYTES: A LESSON FROM DEUTERATION

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INTRODUCTION AND AIM

Histamine H2 receptor is a member of G-protein receptor family, whose binding domain exists in a small pocket within a lipid bilayer. A crucial contribution in the binding of histamine to histamine H2 receptor represents formation of hydrogen bonds between amino acid residues within the third and the fifth transmembrane α-helices (Asp^{98}, Asp^{186} and Tyr^{250}) and three nitrogen atoms of the histamine molecule.

METHODS

In order to estimate the relevance of hydrogen bonds in the process of binding of ligands to H_2 receptor and further on its function, we compared the binding properties of histaminergic ligands to histamine H2 receptor binding sites on cultured neonatal rat astrocytes in control and deuterated medium with the results of quantum chemical calculations. Further on we determined cAMP production upon stimulation with agonist in control and deuterated environment.

RESULTS

Experiments clearly demonstrate that deuteration affects the binding by increasing the affinity for histamine and 4-methylhistamine and reducing the affinity for 2-methylhistamine while basically leaving it unchanged for cimetidine and famotidine. Quantum-chemical calculations on the cluster system extracted from the homology H2 model along with the implicit quantization of the acidic N-H and O-H bonds demonstrate that these changes in the binding can be rationalized by the altered strength of the hydrogen bonding upon deuteration known as the Ubbelohde effect. Deuteration affected the signalling properties of glial H2 receptor, but only when milimolar concentration of histamine was used.

CONCLUSION

The ligand H/D substitution is relevant for therapy in the context of (per)deuterated and thus more stable drugs that are expected to enter therapeutic practice in the near future. Moreover, presented approach may contribute towards understanding receptor activation, while a distant goal remains in silico discrimination between agonists and antagonists based on the receptor structure.

UVODNO PREDAVANJE

KLINIČKA ISPITIVANJA BAZIRANA NA BIOSIMILARIMA U BOSNI I HERCEGOVINI

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UVOD I CILJ

Biosimilari, odnosno biološki slični lijekovi imaju sličnu efikasnost, sigurnost i kvalitet kao već licencirani bio-originatori ali nemaju identičnu hemijsku strukturu. Mogu biti odobreni u svim indikacijama gdje je odobren i bio-originator, čak i bez uzastopnih kliničkih istraživanja [1]. Do sada je od strane Evropske agencije za lijekove (EMA) odobreno 40 biosimilara, a dok su zemlje puput Indije, Kine, Kolumbije i Meksika odobrile kopije etanercepta, a neke latinoameričke zemlje i kopije rituksimaba (ovi biosimilari nisu prošli kroz kompletna istraživanja efikasnosti i mogu pružiti drugačiji stepen efikasnosti, sa nepoznatim profilom sigurnosti, a i veliki su izazov za farmakovigilancu) [2]. Cilj rada je prikaz kliničkih studija na prostoru Bosne i Hercegovine, koje su bazirane na provjeri efikasnosti biosimilara, u četverogodišnjem periodu.

METODE

Rad predstavlja presjek situacije u Bosni i Hercegovini po pitanju kliničkih istraživanja u kojima se ispituje efikasnost biosimilara. Podaci su uzeti iz Registra kliničkih istraživanja Agencije za lijekove i medicinska sredstava Bosne i Hercegovine.

REZULTATI

U periodu 2015.-2018. odobrene su 84 kliničke studije u Bosni i Hercegovini. One su sprovedene ili se sprovode na sekundarnom i tercijarnom nivou zdravstvene zaštite, kao i u privatnim zdravstvenim ustanovama. U istom periodu 4 kliničke studije su registrovane za ispitivanje efikasnosti biosimilara. Dvije ispituju efikasnost biosimilara rituksimaba kod reumatoidnog artritisa, dvije biosimilar bevacizumaba kod karcinoma pluća, a jedna ispituje biosimilar adalimumaba kod Kronove bolesti.

ZAKLJUČAK

S obzirom da biosimilari predstavljaju budućnost (a i već sadašnjost) terapeutskog modaliteta mnogobrojne patologije koja prvenstveno ima lošu prognozu, važno je privlačenje ovog tipa studija u Bosni i Hercegovini, čime bi ova terapija postala dostupna široj populaciji. Razvoj biosimilara i potvrda njihove efikasnosti treba biti put od sveopćeg interesa, uz jasno ciljana klinička istraživanja za potvrdu određenih indikacija, koja će biti sprovedena u skladu sa principima dobre kliničke prakse.

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KLJUČNE RIJEČI: klinička ispitivanja, dobra klinička praksa, biosimilari

CLINICAL TRIALS IN BOSNIA AND HERZEGOVINA BASED ON BIOSIMILARS

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INTRODUCTION AND OBJECTIVE

Biosimilars or biological medicine highly similar to another already approved biological medicine have similar efficacy, safety and quality as already licensed bio-originators but do not have the same chemical structure. They can be approved in all indications where a bio-originator is approved, even without consecutive clinical trials [1]. So far, 40 biosimilars have been approved by the European Medicines Agency (EMA), while countries like India, China, Colombia and Mexico have approved copies of etanercept and some Latin American countries approved copies of rituximab (these biosimilars have not undergone complete efficacy studies, and can provide a different degree of efficacy, with an unknown safety profile, and are also a major challenge for pharmacovigilance) [2]. The aim of this paper is to present clinical studies in Bosnia and Herzegovina based on efficacy testing of biosimilars over a four-year period.

METHODS

This paper presents a cross-section of the situation in Bosnia and Herzegovina in terms of clinical trials that examine the effectiveness of biosimilars. Data were taken from the Clinical Research Registry of the Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina.

RESULTS

In period 2015-2018, 84 clinical studies were approved in Bosnia and Herzegovina. They are or were performed at the secondary and tertiary levels of health care as well as in private health care institutions. In the same period 4 clinical studies were registered that examine the efficacy of biosimilars. Two of them examine the efficacy of rituximab biosimilars in rheumatoid arthritis, two examine biosimilar of bevacizumab in lung cancer, and one examines adalimumab biosimilar in Crohn's disease.

CONCLUSIONS

Considering that biosimilars represent the future (and even the present) of the therapeutic modality of many pathologies, which primarily have poor prognosis, it is important to bring this type of studies to Bosnia and Herzegovina, thus making this therapy available to the general public. The development of biosimilars and the validation of their efficacy should be a path of universal interest, with clearly targeted clinical studies to confirm specific indications, which will be conducted in accordance with the principles of good clinical practice.

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KEY WORDS: clinical trials, good clinical practice, biosimilars

UVODNO PREDAVANJE

VRIJEDNOST NEDJELJE DANA STEČENE TOKOM KLINIČKIH ISTRAŽIVANJA

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UVOD I CILJ

Efikasnost u razvoju i uvodjenju novih lijekova na tržište je važna, kako s etičkog tako i s komercijalnog stanovišta. Novi lijekovi spašavaju živote, donose boljitak pacijenatima i stvaraju dodatne prihode farmaceutskim kompanijama. Prihod generira rast i ponovno investiranje u istraživanje i razvoj novih lijekova. Poznato je međutim da su klinička istraživanja podložna kašnjenjima, veoma često zbog spore regrutacije pacijenata.[1] Cilj ovog članka je da se utvrdi cijena takvih kašnjenja i naglasi važnost njihovog izbjegavanja.

METODE

Da bi ostvario navedene ciljeve, autor je koristio pretragu literature, analize tržišta, kao i sopstveno iskustvo u sprovodjenju kliničkih studija.

REZULTATI

Promet velikih farmaceutskih kompanija mjeri se u milijardama dolara, s prosječnim godišnjim prihodom od $35.4 milijarde za 10 najvećih farmaceutskih kompanija u svijetu u 2018. Ovakav prihod je često rezultat prodaje samo nekoliko jako uspješnih lijekova. Medijan prihoda 15 najprodavanijih lijekova u 2018. je bio $6.9 milijardi. Lijek može zadržati takvu prodaju samo za vrijeme trajanja patenta, jer nakon njegovog isteka u prosjeku se prihodi smanje za oko 40%.[2] Trajanje patenata je fiksno i obično počinje prije nego što lijek uđe u klinička ispitivanja. Prema tome, što je duže istraživanje lijeka, kraći je period do isteka patenta.

ZAKLJUČCI

Kada se uzme u obzir tipični godišnji prihod uspješnog lijeka i smanjenje istog nakon isteka patenta, očigledno je da je vrijednost jedne izgubljene ili stečene sedmice tokom razvoja takvog lijeka oko $54 miliona. U prezentaciji se razmatra značaj uštede vremena i bolje efikasnosti tokom istraživanja lijekova. Takva poboljšanja su imperativ, s obzirom da se rezultirajući prihodi mogu usmjeriti u nova istraživanja, za dobrobit pacijenata i društva u cjelini.

LITERATURA

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[2] EvaluatePharma World Preview 2019, Outlook to 2024. EvaluatePharma Ltd, 12th Edition, June 2019.

KLJUČNE RIJEČI: Kliničko ispitivanje lijekova, prihod lijeka

THE WORTH OF A WEEK GAINED DURING CLINICAL DRUG DEVELOPMENT

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INTRODUCTION AND OBJECTIVE

Getting new drugs to the market efficiently is highly desirable, both from ethical and commercial standpoints. New medicines save lives, improve patients' wellbeing and bring the all-important revenue to pharmaceutical companies. The revenue generates growth and re-investment into the research and development of new compounds. Clinical drug development, however, is liable to delays of which slow patient recruitment is the most common.[1] The aim of this article is to ascertain the cost of such delays and emphasise the importance of avoiding them.

METHODS

To achieve the stated objectives, the author has utilised literature search, market analyses and his own experience in the conduct of clinical trials.

RESULTS

The turnover of large pharmaceutical companies is measured in billions of dollars, with the average annual revenue for the world's top 10 pharmaceutical companies in 2018 being $35.4 billion. This income is often a result of the sales of only a handful of high-grossing drugs by each company. The median revenue for the 15 top-performing drugs in 2018 was $6.9 billion. A drug can only maintain such sales for the duration of its patent because after the patent expires, on average the revenue is slashed by around 40%[2] The patent period is fixed and normally starts before the drug enters clinical trials, hence the longer the drug development, the shorter the patent marketing protection period.

CONCLUSIONS

Considering the typical annual revenue of a blockbuster drug and its reduction after patent expiration, it is evident that the value of a week lost or gained during the development of such a drug is around $54 million. The importance of time- and efficiency-gains in drug research is discussed. Such gains are imperative as the resulting sizable revenue can be channelled into new research for the benefit of patients, and society as a whole.

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KEY WORDS: Clinical drug development, drug revenue

UVODNO PREDAVANJE

RACIONALNA PRIMJENA PERORALNIH INHIBITORA PROTONSKE PUMPE U BOLNIČKOJ I IZVANBOLNIČKOJ PRAKSI

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UVOD

Inhibitori protonske pumpe (IPP) su jedni od načešće korištenih lijekova u medicinskoj praksi. Primjenjuju se parenterealno ili peroralno u liječenju i prevenciji ulkusne bolesti. Peroralni pripravci su osjetljivi na želučanu kiselinu odnosno kiseli medij te moraju imati acidorezistentnu ovojnicu ili neku drugu vrstu zaštite. Također, imaju kratak poluvijek i inhibiraju samo aktivirane protonske pumpe. Zbog toga peroralni IPP zahtijevaju pravovremenu i ispravnu primjenu kako bi ostvarili željeni učinak. U pravilu se uzimaju 30-60 minuta prije obroka. Pogreške na bilo kojoj razini mogu smanjiti djelotvornost IPP [1]. U ovoj studiji smo istražili i usporedili racionalni način primjene IPP kod ambulantnih i hospitaliziranih bolesnika.

METODE

Istraživanje je provedeno na Klinici za unutarnje bolesti s centrom za dijalizu, SKB Mostar i Gradskoj ljekarni Mostar.U istraživanje je uključen 160 bolesnika koji su uzimali IPP. Podatci su dobiveni na osnovu upitnika i medicinske dokumentacije.

REZULTATI

Najveći broj ispitanika u izvanbolničkoj praksi peroralne IPP primjenjuje pravovremeno i na ispravan način (80,43%). Hospitalizirani bolesnici u većoj mjeri nisu pravilno dobivali oralni IPP, samo 41,9% bolesnika je dobilo pravovremeno dok 59,1% ih ga je dobilo nakon obroka.

ZAKLJUČAK

Hospitalizirani bolesnici u većoj mjeri ne dobivaju pravovremno peroralne IPP dok u ambulantnoj praksi većina bolesnika ih uzima na pravilan način.

LITERATURA

[1]. Daniel S. Strand, Daejin Kim, David A. Peura, 25 Years of Proton Pump Inhibitors: A Comprehensive Review. Gut Liver 2017. Jan; 11(1): 27–37.

KLJUČNE RIJEČI: Inhibitori protonske pumpe, racionalna farmakoterapija

RATIONAL USE OF ORAL PROTON PUMP INHIBITORS IN OUTPATIENT AND HOSPITALIZED PATIENTS

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INTRODUCTION

Proton pump inhibitors (PPIs) are one of the most commonly used drugs in medical practice. They are used parenterally or orally in the treatment and prevention of ulcer disease. Oral PPIs preparations are sensitive to gastric acid or acidic medium and they must have an acid resistant coating or some other protection. Also, PPIs have a short half-life and inhibit only activated proton pumps. Therefore, oral PPIs require timely and correct administration to achieve the desired effect. PPIs are usually taken 30-60 minutes before a meal. Errors at any level can reduce the effectiveness of PPIs [1]. In this study, we investigated and compared the rational use of PPIs in outpatient and hospitalized patients.

METHODS

The study was conducted at the Department of Internal Medicine and Dialysis Centre, University Hospital Mostar and The City Pharmacy Mostar. The study included 160 patients taking PPIs. Data were obtained from questionnaires and medical records.

RESULTS

Most outpatients used oral PPIs in a timely and correct manner (80.43%). Hospitalized patients did not receive oral PPIs correctly to a greater extent, only 41.9% of patients received oral PPIs in a timely manner, while 59.1% received oral PPIs after a meal.

CONCLUSION

Hospitalized patients do not receive oral PPIs in a timely manner, while most outpatients receive it properly.

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[1] Daniel S. Strand, Daejin Kim, David A. Peura, 25 Years of Proton Pump Inhibitors: Comprehensive Review. Gut Liver 2017. Jan; 11(1): 27–37.

KEYWORDS: Proton pump inhibitors, rational pharmacotherapy

ORALNA PREZENTACIJA

DIREKTNI (NOVI) ORALNI ANTIKOLAGULANSI (DOACS) – NOVI IZAZOVI U ANTIKOAGULANTNOJ TERAPIJI

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UVOD I CILJEVI

Unatoč otkrivanju i primjeni mnogih antikoagulansnih lijekova, parenteralnih (nefrakcioniranih i niskomolekularnih heparina) i oralnih antagonista vitamina K (VKA), prevencija i liječenje venskih i arterijskih trombotskih događaja i dalje su medicinski izazov [1]. Glavni cilj ovog preglednog rada je predstaviti presjek podataka o direktnim (novim) oralnim antikoagulansima (DOAC), dabigatranu, rivaroksabanu, apiksabanu i endoksabanu.

METODE

U ovom pregledno radu smo: 1. uporedili farmakološke profile DOAC-a s onim varfarina, 2. identificirali doze DOAC-a za svaku odobrenu indikaciju, 3. dali pregled završenih ispitivanja faze III s DOAC-ima, 4. ukratko predstavili studije koje su u toku s DOAC-ima u svrhu odobravanja novih indikacija, 5. dali presjek novih podatke iz svakodnevne prakse s DOAC-ima.

REZULTATI

Najvažnije indikacije DOAC-a su prevencija i liječenje tromboze dubokih vena i plućne embolije, te prevencija trombotskih događaja kod bolesnika s akutnim koronarnim sindromom i atrijalnom fibrilacijom. Različit dozni režim je prilagođen indikaciji. Rezultati većine studija pokazali su više prednosti nego nedostataka za DOAC u poređenju s VKA. Najvažnije prednosti DOAC-a su sigurnost (tj. manja učestalost velikih krvarenja), praktičnost uporabe, manje interakcije lijekova i hrane, širok terapijski raspon i nema potrebe za rutinskim monitoringom.

ZAKLJUČAK

Pokazano je da novi oralni antikoagulansi imaju povoljniji odnos između efikasnosti i sigurnosti u usporedbi s VKA.

LITERATURA

[1] Hinojar R, Jiménez-Natcher JJ, Fernández-Golfín C, Zamorano JL. New oral anticoagulants: a practical guide for physicians. European Heart Journal - Cardiovascular Pharmacotherapy. 2015; 1(2): 134–145.

KLJUČNE RIJEČI: direktni oralni antikoagulansi, atrijalna fibrilacija, moždani udatr

DIRECT (NEW) ORAL ANTICOAGULANT (DOACS) – NEW CHALANGES IN ANTICOAGULANT THERAPY

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INTRODUCTION AND OBJECTIVE
Despite the discovery and application of many parenteral (unfractionated and low-molecular-weight heparins) and oral anticoagulant vitamin K antagonist (VKA) drugs, the prevention and treatment of venous and arterial thrombotic phenomena remain major medical challenges [1]. The main objective of this review is to present recent data on non-vitamin K antagonist oral anticoagulants (DOACs), dabigatran, rivaroxaban, apixaban and endoxaban.

METHODS
In this review we: 1. compared the pharmacological profiles of the DOACs with that of warfarin, 2. identifies the doses of the DOACs for each approved indication, 3. provides an overview of the completed phase III trials with the DOACs, 4. briefly discusses the ongoing studies with the DOACs for new indications, 5. reviews the emerging real-world data with the DOACs.

RESULTS
The most important indications of DOACs are the prevention and treatment of deep vein thrombosis and pulmonary embolisms, and the prevention of thrombotic events in the heart and brain of patients with acute coronary syndrome and atrial fibrillation. Dose-various strengths are available depending on indication. Results of most studies showed more advantages than disadvantages for DOACs when compared with VKAs, with the most important advantages of DOACs including safety issues (ie, a lower incidence of major bleeding), convenience of use, minor drug and food interactions, a wide therapeutic window, and no need for routine monitoring.

CONCLUSION
New oral anticoagulants have shown to have a favorable balance between efficacy and safety compared with VKAs.

LITERATURE:
[1] Hinojar R, Jiménez-Natcher JJ, Fernández-Golfín C, Zamorano JL. New oral anticoagulants: a practical guide for physicians. European Heart Journal - Cardiovascular Pharmacotherapy. 2015; 1(2): 134–145.

KEYWORDS: direct oral anticoagulant, atrial fibrilation, stroke

ORALNA PREZENTACIJA

INHIBITORI EGFR U TERAPIJI NSCLC

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UVOD I CILJ

Receptor epidermalnog faktora rasta (EGFR) je protein - transmembranski receptor. Vezivanjem liganda - epidermalnog faktora rasta (EGF), za ekstracelularni domen EGFR-a dolazi do njegove fosforilacije i aktiviranja. Aktivirani EGFR prenosi fosfornu grupu na tirozinske ostatske celularnih proteina, čime aktivira signalne puteve koji ćeliju vode u diobu i rast. Mutacija onkogena, koji je odgovoran za sintezu EGFR, dovodi do izmjenjene funkcije ovog receptora. Za liječenje nesitnoćelijskog karcinoma pluća (NSCLC) sa mutacijama EGFR onkogena primjenjuju se EGFR-inhibitori - lijekovi koji učestvuju u blokiranju rada EGFR i, posljedično, blokiranju signalnih puteva koji ćeliju vode u nekontrolisanu proliferaciju. Cilj rada bio je ispitati dostupnost EGFR inhibitora u Bosni i Hercegovini (BiH).

METODE

Pregledom literature istraženi su EGFR-inhibitori koji se koriste u terapiji NSCLC-a, a pregledom javno dostupnih podataka Agencije za lijekove i medicinska sredstva Bosne i Hercegovine (ALMBIH) ispitana je dostupnost istih na BiH tržištu.

REZULTATI

U prvu grupu EGFR inhibitora ubrajaju se male sintetske molekule koje su u literaturi označene kao inhibitori tirozin kinaze (TKIs): Erlotinib, Afatinib, Gefitinib, Osimertinib, Dacomitinib... Koriste se kao prva linija liječenja uznapredovalog NSCLC-a, u vidu monoterapije ili u kombinaciji sa hemioterapijom. Kompetativno se vezuju za aktivno mjesto (mjesto fosforilacije EGFR) na intracelularnom djelu ovog receptora.

U drugu grupu ubrajaju se velike biološke molekule – monoklonska antitjela: cetuximab, panitumumab, zalutumumab, nimotuzumab,... Monoklonska antitijela usmjerena su prema antigenu - ekstracelularnom domenu EGFR-a, za koji se vezuje ligand EGF. Primjenjuju se kao prva linija terapije zajedno sa hemioterapijomom.

Trećoj grupi EGFR-inhibitora pripada vakcina kojom se izaziva imuni odgovor pacijenta na ligand EGF. Smanjenjem koncentracije EGF indirektno se smanjuje aktiviranje EGFR-a i nishodno se regulišu prekomjereno aktivirani signalni putevi. Hemijski, lijek predstavlja konjugat humanog rekombinantnog epidermalnog faktora rasta spojenog sa rekombinantnim proteinom rP64K. Primjenjuje se kao druga linija terapije pacijenata sa NSCLC stadijuma IIIB i IV, koji su prethodno završili prvu liniju citostatske terapije bazirane na jedinjenjima platine sa najmanjim odgovorom stabilna bolest i sa bazalnom koncentracijom serumskog EGF≥900 pg/mL [1-3].

ZAKLJUČCI

Na BiH tržištu dostupne su sve navedene terapijske opcije EGFR inhibitora.[8]

LITERATURA

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KLJUČNE RIJEČI: EGF, EGFR inhibitori, NSCLC, dostupnost lijekova

EGFR INHIBITORS IN THERAPY OF NSCLC

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INTRODUCTION

The epidermal growth factor receptor (EGFR) is a protein - transmembrane receptor. Ligand - epidermal growth factor (EGF) are binding at the extracellular domain of EGFR and bring the phosphorylation and activation of observed receptor. Activated EGFR transfers the phosphorus group to tyrosine residues of cellular proteins, thereby activating the signaling pathways that guide the cell into division and proliferation. The mutation of the oncogene, which is responsible for EGFR synthesis, results in altered function of this receptor. EGFR inhibitors are used to treat non-small cell lung cancer (NSCLC) with mutations of the EGFR oncogene. EGFR inhibitors are medicines that participate in blocking EGFR activity and, consequently, blocking signaling pathways leading the cell to uncontrolled proliferation. The aim of this study was to estimate the availability of EGFR inhibitors in Bosnia and Herzegovina (B&H).

METHODE

It was reviewed of the literature regarding EGFR inhibitors which are used in NSCLC therapy and publicly available data from the Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina (ALMBIH) regarding the availability of these on the B&H market.

REZULTATI

The first group of EGFR inhibitors includes small synthetic molecules that have been designated as tyrosine kinase inhibitors (TKIs) in the literature: erlotinib, afatinib, gefitinib, oviertinib, dacomitinib ... They are used as the first line of treatment for advanced NSCLC as monotherapy or in combination with chemotherapy. They bind competitively to the active site (site of the EGFR phosphorylation) at the intracellular part of this receptor.
The second group includes large biological molecules - monoclonal antibodies: cetuximab, panitumumab, zalutumumab, nimotuzumab, ... Monoclonal antibodies are directed to the antigen - the extracellular domain of EGFR, (site of the EGF ligand binds). They are used as the first line of therapy together with chemotherapy.
The third group of EGFR inhibitors is presented as imunotherapy vaccine that provocates immune response of patients to the EGF ligand. Reducing of the the EGF serum concentration observed vaccine indirectly decreases EGFR activation and downregulates overactivated signaling pathways of cells. The vaccine is presented as conjugate of human recombinant epidermal growth factor coupled to the recombinant protein rP64K. It is used as a second-line in the therapy of patients with stage IIIB and IV of NSCLC and who have previously completed the first-line cytostatic therapy based on the platinum compounds with lowest-response as stable disease and with a basal serum EGF concentration ≥900 pg / mL [1-3].

ZAKLJUČCI

All three groups of the EGFR inhibitors which are presented in the literature as therapeutic options for NSCLC are available the BiH market. [8]

LITERATURA

[1] Rodriguez PC, Popa X, Martinez O et al. A Phase III Clinical Trial of the Epidermal Growth Factor Vaccine CIMAvax-EGF as Switch maintenance Therapy in Advanced Non-Small-Cell Lung Cancer Patients. Am Associat Cancer Res 2016; DOI: 10.1158/1078-0432
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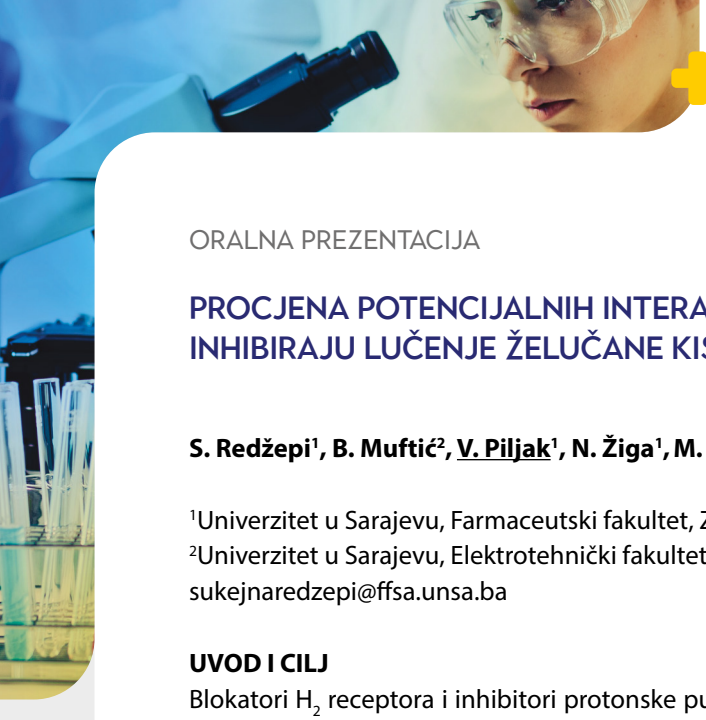
KEY WORDS: EGF, EGFR inhibitors, NSCLC, availability of medicines



ORALNA PREZENTACIJA

PROCJENA POTENCIJALNIH INTERAKCIJA I SIGURNOSTI PRIMJENE LIJEKOVA KOJI INHIBIRAJU LUČENJE ŽELUČANE KISELINE POMOĆU KOMPJUTERSKOG PROGRAMA

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UVOD I CILJ

Blokatori H_2 receptora i inhibitori protonske pumpe su lijekovi koji svoje djelovanje ispoljavaju tako što smanjuju lučenje želučane kiseline. Koriste se u tretmanu gastroezofagealnog refluksa (GERB), želučanog, te duodenalnog ulkusa. Generalno su sigurni lijekovi sa rijetkim neželjenim efekatima i niske toksičnosti, zbog čega su danas jedni od najpropisivanijih lijekova. Međutim, postoje situacije kada stupaju u interakcije sa drugim lijekovima, gdje može doći do promjena u farmakokinetici i farmakodinamici lijekova, što može dovesti do opasnih efekata [1]. Cilj projekta jeste kreirati kompjuterski program koji će farmaceutima poslužiti kao pomoćno sredstvo prilikom izdavanja određenog lijeka pacijentima, a čija glavna uloga će biti predviđanje mogućih interakcija između lijekova i procjena sigurnosti primjene različitih lijekova, naročito kod populacija čija je farmakokinetika i farmakodinamika lijeka izmijenjena.

METODE

Upotrebom C# i MVC obrazca, konstruisan je program koji ispituje moguće interakcije između lijekova i sigurnost primjene odabranog lijeka kod pojedinačih pacijenata.

REZULTATI

Izborom željenih lijekova, kreirani program je sposoban da prepozna da li je odabrana kombinacija lijekova sigurna za upotrebu, opasna, tj. kontraindicirana, ili zahtjeva oprez prilikom primjene. Također, program ima mogućnost da predvidi da li je odabrani lijek siguran za upotrebu kod posebnih populacija ljudi kod kojih je farmakokinetika i farmakodinamika lijeka izmjenjena, kao npr. trudnice, djeca, stariji pacijenti, pacijenti sa bubrežnom insuficijencijom i slično.

ZAKLJUČCI

Program pruža značajne informacije o interakcijama i samoj sigurnosti primjene propisanog lijeka. Bitna osobina programa jeste što omogućava laku i brzu dostupnost informacija, što može biti od velikog značaja prilikom rada u apoteci gdje farmaceut mora brzo procjeniti sigurnost u pogledu primjene propisanih lijekova. Program nije samo namjenjen za farmaceute, već ga mogu koristiti i svi ostali zdravstveni radnici, kao što su doktori, medicinske sestre i slično.

LITERATURA:

[1] Rang HP, Dale MM, Ritter JM, Moore PK. Farmakologija.Beograd, Srbija: Data status, Beograd; 2005

KLJUČNE RIJEČI: interakcije lijekova, posebne populacije, C#, MVC obrazac

THE ASSESSMENT OF DRUG INTERACTIONS AND SAFETY OF ADMINISTRATION OF DRUGS THAT INHIBIT GASTRIC ACID SECRETION BY A DEVELOPED COMPUTER PROGRAM

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INTRODUCTION AND OBJECTIVE

H_2 blockers and proton pump inhibitors are drugs whose main action is decreasing gastric acid secretion. They are used in treatment of gastroesophageal reflux disease (GERD), gastric and duodenal ulcers. These are generally safe drugs with rare adverse effects and low toxicity, which is the reason why they are one of the most frequently prescribed drugs. However, in certain instances they can interact with other drugs, where changes in drug pharmacokinetics and pharmacodynamics and can occur, which can result in dangerous effects [1]. The objective of this project is to create a computer program which will aid a pharmacist during the process of dispensing medication, enabling him to check possible drug interactions and safety of using certain types of drugs when drug pharmacodynamics and pharmacokinetics may be altered.

METHODS

Using C# and MVC pattern, a program was developed which allows the evaluation of drug interactions and safety of administrating the chosen drug to individual patients.

RESULTS

By choosing the drugs of interest, the designed computer program is able to recognize if the given drug combination is safe, dangerous, or if it requires caution during administration. The program is also able to evaluate if the given medication is safe to use in special populations where drug pharmacodynamics and pharmacokinetics are altered, such as pregnant women, children, elderly, patients with kidney insufficiency, etc.

CONCLUSIONS

The application provides significant information regarding the drug interactions and safety of administration of the prescribed drug. Important feature of the program is that it provides information which is easily and instantly available which can have a significant impact whilst working in pharmacy where the pharmacist needs to quickly make a decision regarding the safety of administration of a certain drug. The program can also be used by other health professionals, such as doctors, nurses and others.

REFERENCES

[1] Rang HP, Dale MM, Ritter JM, Moore PK. Farmakologija.Beograd, Srbija: Data status, Beograd; 2005

KEY WORDS: drug interactions, special populations, C#, MVC pattern

ORALNA PREZENTACIJA

KLINIČKA ISPITIVANJA LIJEKOVA U PRAKSI

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UVOD

Lijekovi su često prisutni u našim životima. Da li smo se nekada zapitali zašto baš određeni lijek djeluje kao antibiotik, antihipertenziv ili analgetik? Koliki je razvojni put jednog lijeka od sinteze do primjene na pacijentima? Odgovore, a i konačnu odluku daju upravo rezultati sprovedenih kliničkih ispitivanja na zdravim dobrovoljcima i pacijentima.

CILJ

Ukazati na značaj sprovođenja kliničkih ispitivanja, te šta je sve potrebno znati u slučaju da ste baš vi potencijalni učesnik jednog od kliničkih ispitivanja u BiH.

Šta su to klinička ispitivanja?

Klinička ispitivanja su ispitivanja koja se vrše na ljudima, a imaju za cilj otkrivanje novih i potvrđivanje postojećih terapijskih mogućnosti.

Kako se sprovode klinička ispitivanja

U kliničkim ispitivanjima se lijekovi najčešće ispituju postupkom poređenja sa drugim, već odobrenim lijekovima ili sa placebom. Klinička ispitivanja sprovode se u 4 faze.

Šta je to dobra klinička praksa?

Jasno definisan skup pravila i obaveza svih učesnika kliničkog ispitivanja.

Ko odobrava klinička ispitivanja u BiH?

Prvi stepen su etički komiteti zdravstvenih ustanova u kojima se sprovodi ispitivanje, a potom Agencija za lijekove i medicinska sredstva BiH. Stručnu pomoć pri odobravanju kliničkog ispitivanja daje Komisija za klinička ispitivanja. Odobrenje se daje samo u slučaju da je odnos koristi i rizika pozitivan. Sva odobrena ispitivanja u BiH su javna i dostupna na sajtu Agencije www.almbih.gov.ba

Ko su učesnici u kliničkim ispitivanjima?

Osobe nad kojima se sprovode klinička ispitivanja u BiH su u najvećem broju slučajeva pacijenti, odabrani prema jasno definisanom protokolu ispitivanja, a koji preko svog ljekara specijaliste saznaju za mogućnost učešća u ispitivanju. Ispitanici dobijaju dokument koji se zove Informisani pristanak i u kojem su jasno i razumljivo objašnjeni detalji kliničkog ispitivanja.

Šta je to informisani pristanak?

Informisani pristanak je ključni dokument i neizostavan dio svakog ispitivanja koji osigurava zaštitu pacijenta, učesnika u ispitivanju. Nije dozvoljeno prisiljavanje za učešće u kliničkom ispitivanju. Pacijenti moraju imati dovoljno vremena da se upoznaju sa ispitivanjem prilikom donošenja konačne odluke i potpisivanja informisanog pristanka. Učesnici kliničkog ispitivanja mogu u svakom trenutku, ukoliko smatraju da je opravdano, odustati od ispitivanja.

ZAKLJUČAK

Kliničko ispitivanje za pacijenta predstavlja jedinstvenu priliku da besplatno dobije inovativni lijek. Učesnici u kliničkom ispitivanju ne pomažu samo sebi, već daju veliki doprinos budućim pokolenjima.

LITERATURA

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[2] Pravilnik o kliničkom ispitivanju lijeka i medicinskog sredstva (“Službeni glasnik BiH”, broj: 4/10)
[3] Smjernice dobre kliničke prakse u kliničkom ispitivanju (“Službeni glasnik BiH”, broj: 19/12)

KLJUČNE RIJEČI: kliničko ispitivanje, dobra klinička praksa, učesnici u kliničkim ispitivanjima, informisani pristanak.

CLINICAL TRIALS IN PRACTICE

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INTRODUCTION

Medicines are often present in our lives. Have we ever wondered why a particular drug acts as an antibiotic, antihypertensive or analgesic? What is the developmental pathway of a single drug from synthesis to administration to patients. The answers, and also the final decision, are given precisely by the results of clinical trials conducted on healthy volunteers and patients.

THE GOAL

Point out the importance of conducting clinical trials and what you need to know if you are a potential participant in one of the clinical trials in BiH.

What are the clinical trials?

Clinical trials are human-based trials aimed at discovering new and identifying existing therapeutic options.

How clinical trials are conducted

In clinical trials, drugs are most commonly tested by comparison with other approved drugs or placebo. Clinical trials are conducted in 4 stages.

What is a good clinical practice?

A clearly defined set of rules and obligations for all clinical trial participants.

Who approves clinical trials in BiH?

The first instance is the ethics committees of the health institutions undergoing the testing, followed by the BiH Agency for Medicinal Products and Medical Devices. Expert assistance in the approval of the clinical trial is provided by the Clinical Trials Commission. Approval is only given if the benefit / risk balance is positive. All approved examinations in BiH are public and available on the Agency's website www.almbih.gov.ba

Who are participants in clinical trials?

Persons undergoing clinical trials in BiH are in most cases patients, selected according to a clearly defined test protocol, who, through their specialist physician, learn about the possibility of participating in the trial. Respondents are provided with a document called Informed Consent explaining clearly and understandably the details of the clinical trial.

What is an informed consent?

Informed consent is a key document and an indispensable part of any trial that ensures the protection of the patient, the trial participant. Compulsion to participate in a clinical trial is not permitted. Patients must have sufficient time to familiarize themselves with the examination when making their final decision and signing informed consent. Clinical trial participants may withdraw from the trial at any time if they consider it warranted.

CONCLUSION

The clinical trial for the patient represents a unique opportunity to receive an innovative drug for free
Participants in the clinical trial are not only helping themselves, but are making a major contribution to future generations.

LITERATURE

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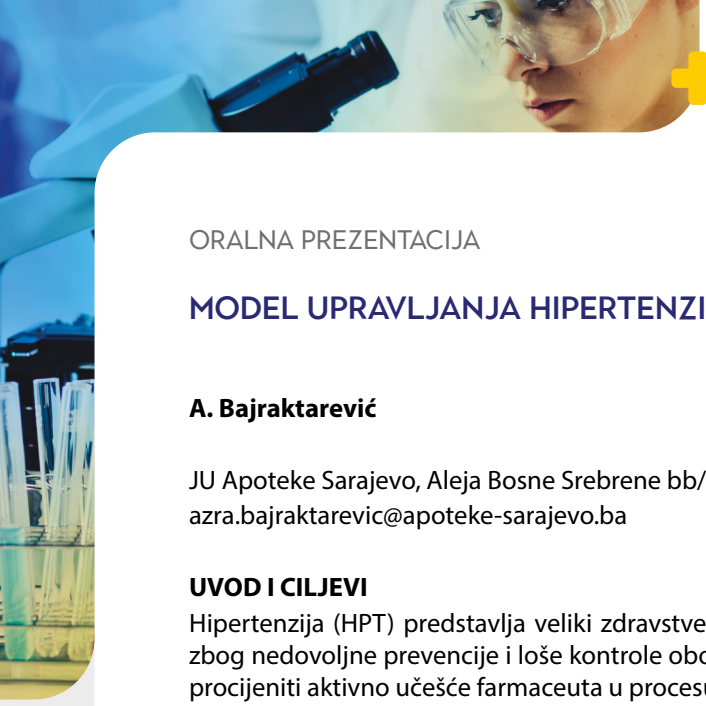
[2] Rulebook on Clinical trials of Medicinal products and Medical devices ("Official Gazette BiH", number: 4/10)
[3] Guidelines on Good clinical practice ("Official Gazette BiH", number: 19/12)

KEYWORDS: clinical trial, good clinical practice, participants in clinical trials, informed consent.



ORALNA PREZENTACIJA

MODEL UPRAVLJANJA HIPERTENZIJOM U APOTECI: PRILIKE I ODGOVORNOSTI

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UVOD I CILJEVI

Hipertenzija (HPT) predstavlja veliki zdravstveni problem u većini država uključujući i Bosnu i Hercegovinu zbog nedovoljne prevencije i loše kontrole oboljenja na nivou primarne zdravstvene zaštite. Cilj studije je bio procijeniti aktivno učešće farmaceuta u procesu brige za pacijenta u upravljanju HPT-om u apoteci.

ISPITANICI I METODE

Prospektivna studija presjeka, provedena je tokom kampanje promocije zdravlja i prevencije bolesti, na uzorku koji su činili korisnici usluga JU "Apoteke Sarajevo". Intervju s pacijentom, koji je izrazio želju da izmjeri krvni tlak, uz istovremeni skrining ostalih faktora rizika je proveden u kutku za razgovore korištenjem namjenski kreiranog upitnika za potrebe ove studije. Istovremeno su praćene redovne dnevne aktivnosti farmaceuta u procesu izdavanja lijekova za tretman hipertenzije. Na vidnom mjestu su istaknuti posteri o značaju kontrole krvnog tlaka.

REZULTATI

Studija presjeka završena je s 553 ispitanika i detektovan je povišen krvni tlak u ispitanika sa potvrđenom dijagnozom hipertenzije u odnosu na ispitanike koji nemaju spoznaju o hipertenziji 40.2% vs 17.3%. Svim ispitanicima su dati savjeti o zdravim životnim navikama, a posebno odraslim osobama sa nepovoljnim profilom kardiovaskularnog rizika (gojaznost, životna dob, nezdrava prehrana, fizička neaktivnost, određeni lijekovi). U praksi izdavanja antihipertenzivne terapije, pacijentima je obezbjeđeno savjetovanje o terapiji i nefarmakološkim mjerama, usmeno i po potrebi uz detaljne pismene instrukcije.

ZAKLJUČAK

U provedenom istraživanju u JU "Apoteke Sarajevo" ustanovljen je evidentan potencijal farmaceuta da identificira pacijente sa povećanim faktorima rizika od hipertenzije, te da svojim stručnim intervencijama da podršku sistemskim mjerama u kontroli hipertenzije. Zahtjeva se plan za povećanje praćenja adherencije pacijenata.

KLJUČNE RIJEČI: hipertenzija, javne apoteke, farmaceut

MODEL OF HYPERTENSION MENAGEMENT IN PHARMACY: OPORTUNITIES AND RESPONSIBILITIES

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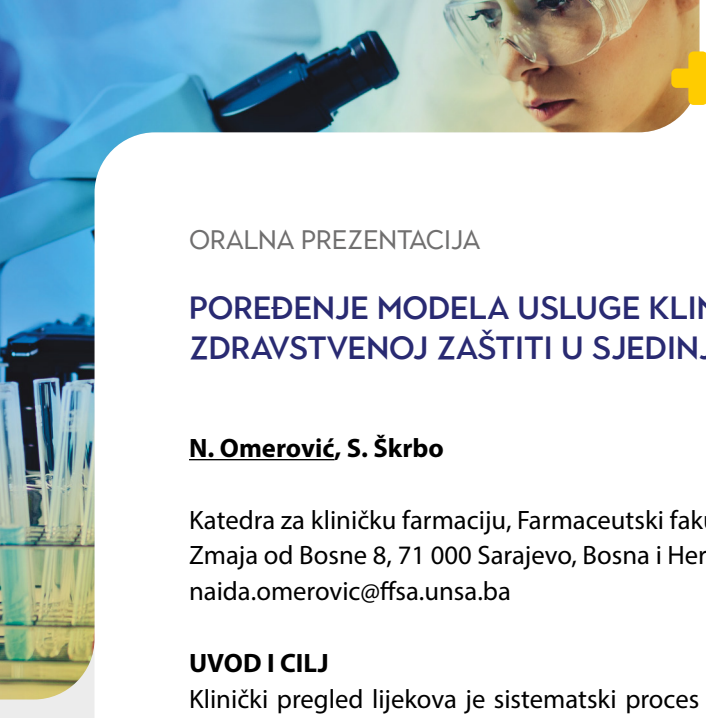
INTRODUCTION
Hypertension (HTN) is a major health issue in most countries, including Bosnia and Herzegovina, due to insufficient preventive measures and poor disease control at the primary care level. The aim of the study was to evaluate the active participation of pharmacists in the patient care process in the management of HTN in pharmacy.

SUBJECT AND METHOD
A prospective cross-sectional study was conducted during a health promotion and disease prevention campaign, based on a sample of customers of Public Institution "Apoteke Sarajevo". An interview with a patient, who wished to measure his blood pressure, while also performing a screening of other risk factors, was conducted in the private consultation area using a set of questions from a dedicated questionnaire for the purpose of this study. At the same time, the daily activities of pharmacists in the process of dispensing hypertension medications were monitored. Posters containing brief information on the importance of high blood pressure control were displayed in pharmacy.

RESULTS
The cross-sectional study was completed with 553 subjects and high blood pressure was detected in subjects with a confirmed diagnosis of hypertension compared to those subjects who were not aware that they suffer from hypertension, 40.2% vs 17.3%. All subjects were advised how to adopt healthy lifestyle habits, especially adults with unfavourable cardiovascular risk profile (obesity, age, unhealthy diet, physical inactivity, and certain medications). In the process of dispensing antihypertensive medications, patients are personally advised about their treatment and non-pharmacological measures, and if necessary, detailed written instructions are provided.

CONCLUSION
The conducted study revealed the evident potential of pharmacists to identify patients with increased risk for developing hypertension and to implement systemic measures to control hypertension, according to their willingness and professional interventions. A plan to increase the monitoring of patient adherence/compliance is required.

KEY WORDS: hypertension, community pharmacy, pharmacists



ORALNA PREZENTACIJA

POREĐENJE MODELA USLUGE KLINIČKOG PREGLEDA LIJEKOVA U PRIMARNOJ ZDRAVSTVENOJ ZAŠTITI U SJEDINJENIM AMERIČKIM DRŽAVAMA I AUSTRALIJI

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UVOD I CILJ

Klinički pregled lijekova je sistematski proces prikupljanja podataka o pacijentu, procjene njegove terapije, identifikacije problema u vezi s terapijom, izrade plana za rješavanjeproblema u skladu s prioritetima, u saradnji s pacijentima.Cilj ovog rada je uporediti dva u svijetu najrazvijenija modela usluge kliničkog pregleda lijekova:u Sjedinjenim Američkim Državama i Australiji.

METODE

Sistemsko pretraživanje stručne i naučne literature, baza podataka (*PubMed*, *Medline*, *EBSCO*, *Science Direct*), elektronskih časopisa i knjiga, preko općih i specijaliziranih pretraživača (*Google*, *Google Scholar*), korištenjem ključnih riječi.

REZULTATI

U Sjedinjenim Američkim Državama je razvijen model *Upravljanje terapijom*(eng. *Medication Therapy Management*; *MTM*), u kojeg su uključeni pacijenti koji boluju od više hroničnih bolesti, koriste više lijekova i izdvajaju više novca za zdravstvenu zaštitu. On obuhvata pet elemenata: *pregled terapije*, *ličnu evidenciju lijekova*, *terapijski akcioni plan*, *intervencije i upućivanje ljekaru* i *dokumentaciju i praćenje*. Pacijentima koji ispunjavaju kriterije se usluga kliničkog pregleda lijekova pruža jednom godišnje, a praćenje ishoda terapije jednom u tri mjeseca, kroz ciljane preglede terapije. Model u Australiji podrazumijeva da pacijenti, da bi bili uključeni u program, koriste više od pet lijekova, sveukupno 12 doza dnevno, imaju dijagnosticirane najmanje tri bolesti, iz bolnice su otpušteni u prethodnih mjesec dana, u posljednja tri mjeseca su imali znatnije promjene u terapiji, koriste lijekove uske terapijske širinekoji zahtijevaju terapijski monitoring ili imaju simptome neke neželjene reakcije na lijek ili izostanka efikasnosti terapije. Usluga kliničkog pregleda lijekova se pruža u domovima pacijenata i domovima za stare osobe, a praćenje ishoda terapije u apoteci. Terapijski plan u ovom modelu podrazumijeva kombinaciju *lične evidencije lijekova* i *terapijskog akcionog plana* iz američkog modela.

ZAKLJUČCI

Oba modela, iako specifična po kriterijima uključivanja pacijenata te mjestima obavljanja i strukturi usluge kliničkog pregleda lijekova, imaju iste osnovne principe: inkorporiranje svih koraka farmaceutske zdravstvene zaštite u jedan model i obezbjeđivanje efikasne i sigurne zdravstvene zaštite pacijenata.

KLJUČNE RIJEČI: model usluge, klinički pregled lijekova, primarna zdravstvena zaštita, Sjedinjene Američke Države, Australija

COMPARISON OF CLINICAL MEDICATION REVIEW SERVICE MODELS IN PRIMARY HEALTH CARE IN THE UNITED STATES AND AUSTRALIA

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INTRODUCTION AND AIM
Clinical medication review is a systematic process of collecting patient data, evaluating his therapy, identifying therapy problems, making a problem-solving plan based onpriorities, in collaboration with patients. The objective of this paper is to compare the two most developed clinical medication review service models in the world: in the United States and Australia.

METHODS
Systematic research of scholarly and scientific literature, databases (*PubMed*, *Medline*, *EBSCO*, *Science Direct*), electronic journals and books, via general-purpose and specialized search engines (*Google*, *Google Scholar*), using keywords.

RESULTS
Medication Therapy Management (*MTM*) model was developed in the United States, involving patients who suffer from multiple chronic diseases, use multipledrugs and issue larger amounts of money for health care. This model has five elements: *medication therapy review*, *personal medication record*, *medication-related action plan*, *interventions and referrals* and *documentation and follow-up*. Patients who meet these criteria are provided with clinical medication review service once a year and follow-up service once every three months, via targeted medication reviews. Australian model implies that, in order to be included, patients use more than five drugs, a total of 12 doses per day, were diagnosed with at least three diseases, were discharged from the hospital in the previous month, in the last three months had significant changes in therapy, usedrugsof narrow therapeutic index that require therapeutic monitoring or have symptoms ofsome adverse reactions or lack of drugefficacy.Clinical medicationreview serviceis provided atpatients' homes and nursing homeswhilstfollow-upservice at the pharmacy. The therapeutic plan is a combination of *personal medication record* and *medication-related action plan*.

CONCLUSIONS
Both models, although having specific patient-inclusion criteria, place of provision and structure of clinical medication review service, have similar basic principles: incorporating all steps of pharmaceutical care in one model and providingefficient and reliablehealth care.

KEYWORDS: servicemodel, clinical medication review, primary health care, the United States, Australia

ORALNA PREZENTACIJA

ORIGINALNI VS GENERIČKI LEKOVI – STAVOVI, MIŠLJENJA I PRAKSA LEKARA

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UVOD I CILJ

Upotreba generičkih lekova (GL) u značajnom je porastu. Brojne studije koje istražuju ovu oblast govore u prilog bezbednosti, efikasnosti i kvaliteta GL, odnosno terapijskoj ekvivalenciji sa originalnim lekovima (OL), ali i o podeljenosti stavova zdravstvenih profesionalaca po istom pitanju [1]. Cilj istraživanja jeste analiza mišljenja i stavova lekara o GL i OL reflektovanim kroz njihovu propisivačku praksu.

METOD

U studiju preseka tokom 2019. uključeni su nasumično odabrani lekari iz zdravstvenih ustanova primarnog, sekundarnog i tercijarnog nivoa zdravstvene zaštite u Vojvodini. Za potrebe istraživanja kreiran je namenski upitnik. Učešće u studiji bilo je dobrovoljno i anonimno.

REZULTATI

Zamenu OL sa GL uvek podržava 23% ispitanika, 29,5% je često za tu opciju, dok bi 13,5% retko, a 17,5% nikada ne bi zamenilo OL sa GL. U svojoj praksi 52% ispitanika se susrelo sa razlikom u efikasnosti GL i OL. Sa izjavom da su GL lošijeg kvaliteta u odnosu na OL, mišljenja su vrlo dispergovana, od 13% koji se potpuno slažu, 21% koji se delimično slažu, do 16% odnosno 30% koji delimično ili potpuno ne podržavaju ovu tvrdnju, a 20% nije iznelo svoje mišljenje. Svega 5,5% ispitanika se u potpunosti slaže sa izjavom da GL izazivaju više neželjenih dejstava nego OL, dok 85% veruje u podjednaku bezbednost obe grupe lekova [2].

ZAKLJUČCI

Većina lekara veruje u bezbednost i kvalitet GL, kao i da oni neće izazvati više neželjenih dejstava u poređenju sa originalnim lekom. Međutim, postoje značajne razlike u pogledu načina na koji zdravstveni radnici posmatraju efikasnost GL i terapijsku ekvivalentnost sa OL. Kontinuirana edukacija zasnovana na dokazima, transfer znanja i interprofesionalna saradnja uz nastavak istraživanja ove oblasti ubuduće može obezbediti harmonizaciju znanja, stavova i prakse zdravstvenih profesionalaca.

LITERATURA

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KLJUČNE REČI: originalni lekovi, generički lekovi, terapijska ekvivalentnost, propisivačka praksa

ORIGINAL VS GENERIC DRUGS – ATTITUDES, OPINIONS AND DOCTORS` PRACTICE

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INTRODUCTION AND AIM

Use of generic drugs (GD) constantly increases. Many studies on this topic claim safety, efficiency and quality of GD, and that they are therapeutic equivalents with original drugs (OD), but there are still different opinions of health care professionals on this matter [1]. Aim of this study is to analyze doctors' opinions and attitudes on GD and OD through their prescribing practice.

METHODS

This cross-sectional study conducted during 2019 included randomly selected physicians from from all three levels of health care in Vojvodina. Data were collected by a specially designed questionnaire. Participation in the study was voluntary and anonymous.

RESULTS

Switch from OD to GD was supported always 23% respondents, often by 29,5%, rarely by 13,5% and 17,5% would never change OD with GD. 52% respondents reported that they have noticed diferrences in efficiency between GD and OD. There are very dispersed opinions about statement that GD are of lower quality than OD, from 13% respondents who completely agree, 21% who partially agree, to 16% and 30% who partially or completely disagree with this statement, while 20% respondents did not declare. Only 5,5% respondents completely agree that GD cause adverse effects more often than OD, while 85% think consider that GD and OD have similar safety [2].

CONCLUSIONS

Most respondents think that GD are safe and efficient, and that they would not cause more adverse effects than OD. However, there are significant differences in the way how health care professionals interpret efficiency and therapeutic equivalence between GD and OD. Evidence based continual education, transfer of knowledge and interprofessional cooperation with further research on this topic could provide harmonization of knowledge, attitudes and practice of health care professionals.

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KEY WORDS: original drugs, generic drugs, therapeutic equivalents, prescribing practice

ISPITIVANJE UTICAJA NOVOSINTETISANIH KSANTEN-3-ONA NA HEMATOLOŠKI STATUS ŠTAKORA

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UVOD I CILJEVI

Ksanteni su heterociklični spojevi, prirodnog i sintetskog porijekla, koji su zbog svojih farmakoloških osobina izuzetno interesantni za ispitivanja. Do sada je dokazano njihovo antiinflamatorno, antioksidativno, antibakterijsko i antifungalno[1- 3] djelovanje. U ovom radu ispitivano je djelovanje novosintetisanih ksantena: 2,6,7-trihidroksi-9-(2-hidroksi-5-bromofenil)-3H-ksanten-3-on (SPOJ1) i 2,6,7-trihidroksi-9-(3-bromofenil)-3H-ksanten-3-on (SPOJ 2) na hematološki status štakora nakon intramuskularne primjene. Ispitivane su promjene na neutrofilima, eozinofilima, bazofilima, limfocitima, monocitima, target ćelijama, stomatocitima, sferocitima, ovalocitima, retikulocitima, anulocitima, šizocitima, akantocitima, ehinocitima, siderocitima i dakriocitima.

METODE

U studiji je korišteno 12 štakora, po 6 za svaki spoj, soj Wistar, starosti 2-3 mjeseca, prosječne težine 180-250 g. Spojevi 1 i 2 su davani intramuskularno jednom dnevno u koncentraciji 0,156 mg/ml. Krv štakora je punktirana iz repne vene nakon 7 i 14 dana primjene. Analizirano je 2000 eritrocita i leukocita, a poikilociti su evidentirani oslanjajući se na standardnu morfologiju. Poikilocitoza je klasificirana semikvantitativno kao nepostojeća (0%), rijetka (0,05-0,5%), blaga (0,5 – 3%), umjerena (3 – 10%) i izražena (>10%). Statistička obrada rezultata je vršena u programu IBM SPSS Statistics 25.0.

REZULTATI

Nakon statističke obrade podataka, uočeno je da postoji statistički značajna razlika ($p<0,05$) u nivoima limfocita, monocita, stomatocita, retikulocita, anulocita i dakriocita nakon primjene oba spoja, dok je kod sferocita značajna razlika nakon primjene prvog spoja, a kod ovalocita nakon primjene drugog spoja.
Poikilocitoza je blaga do umjerena, a najveća je bila kod anulocita nakon primjene prvog spoja (9,05%).

ZAKLJUČCI

Iako ksanteni u *in vitro* ispitivanjima pokazuju dobra farmakološka djelovanja,neophodna su temeljitija ispitivanja njihove toksičnosti i uticaja na druge sisteme. Abnormalne vrijednosti crvenih i bijelih krvnih zrnaca, kao i trombocita, često ukazuje na oboljenja kao što su anemije, limfomi, leukemije, kanceri bubrega i pluća, tako da je ova vrsta pretraga od izuzetne važnosti.

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KLJUČNE RIJEČI: ksanten, eritrociti, poikilocitoza

TESTING THE EFFECTS OF NEWLY SINTETIZED XANTHEN-3-ONON HEMATOLOGICAL STATUS IN RATS

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INTRODUCTION

Xanthenes are heterocyclic compounds of natural and synthetic origin, which, because of their pharmacological properties, are of great interest for testing. So far, their anti-inflammatory, antioxidant, antibacterial and antifungal activity has been demonstrated [1 - 3]. The effect of newly synthesized xanthenes: 2,6,7-trihydroxy-9- (2-hydroxy-5-bromophenyl) -3H-xanten-3-one (Compound 1) and 2,6,7-trihydroxy-9 was investigated in this paper - (3-bromophenyl) -3H-xanten-3-one (Compound 2) on the hematological status of rats after intramuscular administration. Changes in neutrophils, eosinophils, basophils, lymphocytes, monocytes, target cells, stomatocytes, spherocytes, ovalocytes, reticulocytes, anisocytes, schizocytes, acantocytes, echinocytes, siderocytes and dacryocytes were examined.

METHODS

The study used 12 rats, 6 for each compound, Wistar strain, 2 - 3 months old, with an average weight of 180 - 250 g. Compounds 1 and 2 were administered intramuscularly once daily at a concentration of 0,156 mg / ml. Rat blood was punctured from the tail vein after 7 and 14 days of administration. 2000 erythrocytes and leukocytes were analyzed and poikilocytes were recorded based on standard morphology. Poikilocytosis was classified semi-quantitatively as nonexistent (0%), rare (0,05 – 0,5%), mild (0,5 - 3%), moderate (3 - 10%) and expressed (> 10%). Statistical analysis of the results was performed in IBM SPSS Statistics 25.0.

RESULTS

After statistical analysis, it was observed that there was a statistically significant difference ($p < 0,05$) in the levels of lymphocytes, monocytes, stomatocytes, reticulocytes, anulocytes and dacryocytes after administration of both compounds, whereas in spherocytes there was a significant difference after administration of the first compound, and in ovalocytes after administration of the second compound.

Poikilocytosis was mild to moderate and was highest in anulocytes after administration of the first compound (9,05%).

CONCLUSIONS

Although xanthenes have shown good pharmacological effects in in vitro studies, more thorough studies of their toxicity and effects on other systems are necessary. Abnormal values of red and white blood cells, as well as platelets, often indicate diseases such as anemia, lymphomas, leukemias, kidney and lung cancers, so this type of search is of the utmost importance.

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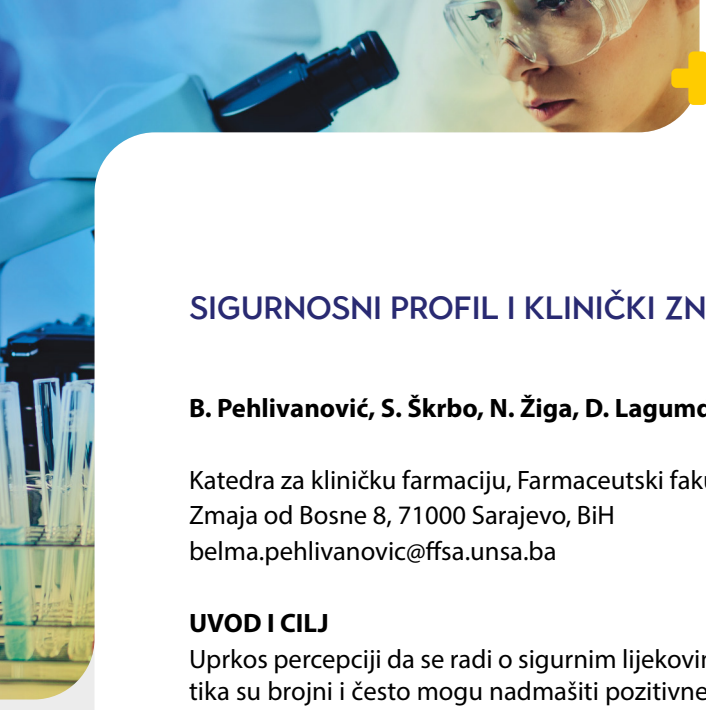
KEY WORDS: xanthen, red blood cells, poikilocytosis



SIGURNOSNI PROFIL I KLINIČKI ZNAČAJNE INTERAKCIJE OTC ANALGETIKA

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UVOD I CILJ
Uprkos percepciji da se radi o sigurnim lijekovima, neželjeni efekti i interakcije najčešće izdavanih OTC analgetika su brojni i često mogu nadmašiti pozitivne učinke njihove primjene. Stoga, svaki odobreni lijek, neovisno o tome izdaje li se na recept ili ne, mora zadovoljiti postavljene stroge zahtjeve kvaliteta, sigurnosti i djelotvornosti. U radu je predstavljen prikaz najčešćih neželjeni efekata i klinički značajnih interakcija usljed primjene bezreceptnih analgetika.

METODE
Izvršen je retrospektivni i deskriptivni tip istraživanja uz korištenje dostupnih baza podataka.

REZULTATI
Neželjeni efekti bezreceptnih analgetika često su posljedica njihove nepropisne primjene, uključujući i istovremeno uzimanje s drugim skupinama lijekova, te se najčešće manifestiraju na gastrointestinalnom traktu, bubrezima, jetri i koži. Poremećaji od strane gastrointestinalnog trakta izazvani bezreceptnim analgeticima uključuju dispepsiju, ezofagitis, ezofagealne strikture, gastritis, gastrične i duodenalne petehije, erozije, ulceracije, krvarenja i perforacije tankog i debelog crijeva, te egzacerbacije hroničnih inflamatornih bolesti debelog crijeva. Hepatotoksičnost je u najvećem broju slučajeva zabilježena usljed hronične primjene bezreceptnih lijekova, dok do akutnog oštećenja jetre dolazi tek u slučajevima predoziranja s ovim lijekovima. Ozbiljne kožne reakcije, neke od njih i sa smrtnim ishodom, uključujući eksfolijativni dermatitis, Stevens-Johnsonov sindrom i toksičnu epidermalnu nekrolizu, zabilježene su vrlo rijetko pri primjeni nesteroidnih antiinflamatornih lijekova. Izdavanjem lijeka bez recepta pacijentima se osigurava brža i lakša dostupnost ali pod uvjetom da lijek zadovoljava stroge uvjete za takav način izdavanja i uz neophodnu stručnu procjenu magistra farmacije.

ZAKLJUČCI
Iako su OTC analgetici svrstani među sigurnije lijekove, njihova upotreba nosi određen rizik od neželjenih dejstava. Zadatak je farmaceuta da iskoriste svoje stečeno znanje s ciljem smanjivanja potencijalnih rizika od nastanka neželjenih pojava i interakcija kod pacijenata za koje znaju da koriste bezreceptne analgetike.

KLJUČNE RIJEČI : samomedikacija, bezreceptni analgetici, neželjeni efekti, interakcije.

SAFETY PROFILE AND CLINICALLY SIGNIFICANT INTERACTIONS OF OTC ANALGETICS

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INTRODUCTION AND AIM
Despite the perception that OTC analgetics are safe medicines, the side effects and interactions of commonly prescribed OTC analgetics are numerous and can often outweigh the positive effects of their use. Therefore, every approved drug, whether or not it is prescribed, must meet the strict requirements of quality, safety and efficacy. This paper presents a summary of the most common side effects and clinically relevant interactions resulting from the use of non-prescription analgetics.

METHODS
A retrospective and descriptive type of survey was conducted using available databases.

RESULTS
The side effects of non-prescription analgetics are often the result of their improper use, including co-administration with other drug groups, and are most commonly manifested in the gastrointestinal tract, kidneys, liver and skin. Gastrointestinal disorders caused by non-prescription analgetics include dyspepsia, esophagitis, esophageal strictures, gastritis, gastric and duodenal petechiae, erosion, ulceration, bleeding and perforation of the small and large intestine, and exacerbations of chronic debridement. Hepatotoxicity has been reported in most cases due to the chronic use of non-prescription drugs, whereas acute liver damage occurs only in cases of overdose with these drugs. Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely with the use of non-steroidal anti-inflammatory drugs. The dispensing of an over-the-counter medication provides patients with faster and easier availability, but only when that drug meets the strict conditions for such dispensing and with the necessary expert judgment of the pharmacists.

CONCLUSION
Although OTC analgetics are classified as safe medicines, their use carries certain risk of side effects. It is the task of pharmacists to utilize their acquired knowledge with the aim of reducing the potential risk of adverse effects and interactions in patients who are known to use over-the-counter analgetics.

KEY WORDS: self-medication, OTC analgetics, side effects, interactions

INOVATIVNI PRISTUP U TERAPIJI MULTIPLE SKLEROZE

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UVOD I CILJEVI

Multipla skleroza (MS) je autoimuna demijelinizirajuća bolest koja djeluje na centralni nervni sistem i dovodi do oštećenja mozga i kičmene moždine. Trenutna terapija MS ima za cilj da uspori progresiju oboljenja i da smanji stopu godišnjih relapsa. Ciljevi ovoga rada su istražiti potencijalne terapijske puteve kao i nove lijekove u tretmanu MS.

METODE

U svrhu postizanja navedenih ciljeva kao izvor podataka korištena je dostupna stručna i naučna literatura, medicinske baze podataka, internet, opći i dubinski pretraživači.

REZULTATI

Biološka terapija predstavlja inovativni terapijski pristup koji uključuje imunoterapiju (vakcine, aferezu i antitijela) ; gensku terapiju; i transplantaciju matičnih ćelija. Reparacija antigen-specifične tolerancije putem vakcinacije jedan je od novih pristupa u terapiji MS. Antigen-specifična vakcinacija je usmjerena na izmijenjeni imuni odgovor protiv specifičnih antigena koji su povezani sa bolešću uz istovremeno održavanje kapaciteta imunog sistema da odgovori na antigene koji nisu povezani za oboljenjem. Monoklonalna antitijela su potentni imunosupresivni lijekovi koji se nazivaju "terapije koje modificiraju bolest" (eng. "*disease-modifying therapies*"). Natalizumab je postao prvo odobreno monoklonalno antitijelo za tretman relapsne MS nakon što je pokazao značajnu kliničku efikasnost u dvije velike studije. U radu je dat prikaz potencijalnih humaniziranih antitijela u terapiji MS koja su još uvijek u fazi istraživanja. Imunoablativna terapija je predložena kao tretman imunološki-posredovanih bolesti poput MS. Koncept se sastoji iz resetiranja imunološke memorije usmjerene protiv autoantigena. Autologna hematopoetska transplantacija matičnih ćelija je evaluirana u nekoliko stotina pacijenata koji boluju od MS i za sada je odobrena njena primjena samo u domenu kliničkih ispitivanja.

ZAKLJUČAK

Biološka terapija predstavlja prvi korak ka personaliziranoj terapiji i otvara mogućnost za potencijalnu reparaciju tkiva i neuroregeneraciju primjenom gena ili ćelijske terapije. Kako rastu indikacije za primjenu biološke terapije bitno je procijeniti efikasnost i rizik. Trenutno se odvijaju brojna istraživanja čiji rezultati će pomoći u boljem razumijevanju i primjeni ovih lijekova.

KLJUČNE RIJEČI: multipla skleroza, monoklonalna antitijela, biološki lijekovi

INNOVATIVE THERAPEUTICAL APPROACHES IN MULTIPLE SCLEROSIS

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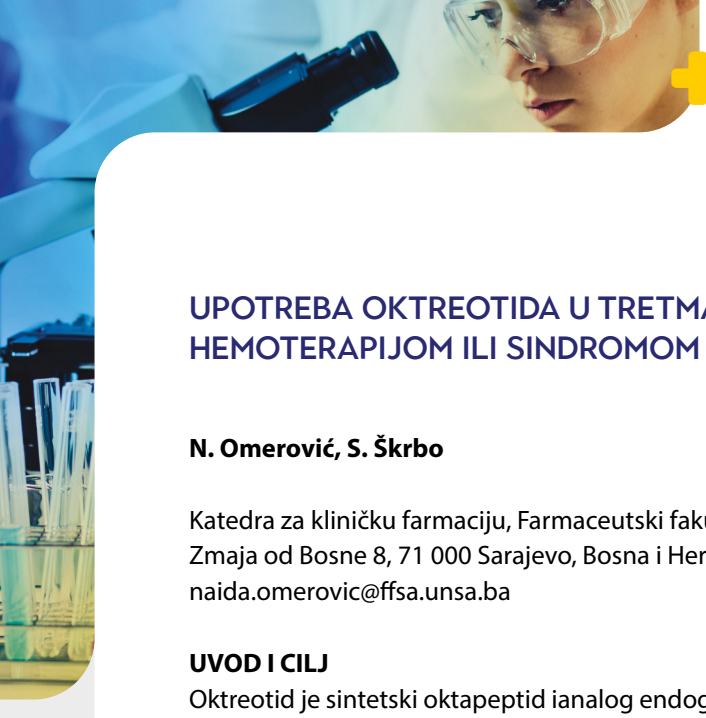
INTRODUCTION AND AIMS
Multiple sclerosis (MS) is autoimmune demyelinating disease which affects central nervous system and results with brain and spinal cord damage. Current approved therapy for MS has a goal to slow progression of the disease and to reduce annual relapse rate number. The objective of this paper is to investigate potential new therapeutic pathways and new medicines in treatment of MS.

METHODS
For the purpose of achieving these aims, available professional and scientific literature, medical databases, Internet, general and deep search engine, were used as data sources.

RESULTS
Biological therapy is innovative approach for treatment MS and it includes immunotherapy (vaccines, apheresis and antibodies) ; gene therapy and stem cells transplantation. Reparation of antigen-specific tolerance using vaccine is one of new approaches in treatment of MS. Antigen-specific vaccination is directed on the changed immune system response against specific antigens, which are connected with the disease, at the same time maintaining capacity of immune system to react on antigens which are not connected with the disease. Monoclonal antibodies are potency immunosuppressive medicines that are named "disease-modifying therapies". Natalizumab demonstrate significant clinical efficacy in two large studies and become first approval monoclonal antibody for treatment of relapse-MS. This paper describes potential humanized antibodies in therapy of MS that are in different stages of clinical trials. Immune ablative therapy is proposed as a treatment of immune-mediated disease as MS. The concept consists of resetting immune memory against autoantigens. Stem cells transplantation is evaluated in few hundred of patients with MS, and so far it is allowed to be used only in domain of clinical trials.

CONCLUSION
Biological therapy represents the first step in personalized therapy and gives opportunity for potential reparation of tissue and neuroregeneration using genes or stem cells therapy.As the indications for use of biological therapy grow, it is important to evaluate the effectiveness and risk. Great number of studies are currently underway that will help better understanding and applying of these medicine.

KEY WORDS: multiple sclerosis, monoclonal antibodies, biological drugs



UPOTREBA OKTREOTIDA U TRETMANU REFRAKTORNE DIJAREJE UZROKOVANE HEMOTERAPIJOM ILI SINDROMOM STEČENE IMUNODEFICIJENCIJE

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UVOD I CILJ

Oktreotid je sintetski oktapeptid ianalog endogenog somatostatina,akoristi se u tretmanu karcinoida i tumora koji luče vazoaktivni intestinalni peptid (eng. *Vasoactive Intestinal Peptide*; *VIP*). On blokira oslobađanje različitih peptidate usporava gastrointestinalni motilitet i intestinalnu apsorpciju.Refraktorna dijareja traje duže od 14 dana, nema odgovora na primjenu antidijaroika (loperamida), a najčešća je kod pacijenata na hemoterapiji ilisa dijagnosticiranim sindromom stečene imunodeficijencije (eng. *Acquired Immunodeficiency Syndrome*; *AIDS*). Cilj ovog rada je evaluirati saznanja o upotrebi oktreotida u tretmanu refraktorne dijareje, te prednostima i nedostacima iste.

METODE

Sistemsko pretraživanje stručne i naučne literature, baza podataka (*PubMed*, *Medline*, *EBSCO*, *Science Direct*), elektronskih časopisa i knjiga, preko općih i specijaliziranih pretraživača (*Google*, *Google Scholar*), korištenjem ključnih riječi.

REZULTATI

U studijama u kojima je ispitivana mogućnost upotrebe oktreotida u tretmanu refraktorne dijareje kod pacijenata na hemoterapiji ili sa AIDS-om, korištene su doze 50-5000 µg subkutano ili intravenozno. Njegova efikasnost je procijenjivana preko zapremine stolice i ukupno apsorbovane tečnosti. Pokazao se efikasnijim u tretmanu refraktorne dijareje kod pacijenata na hemoterapiji (potpuni odgovor: 86-96%) nego kod onih sa AIDS-om (potpuni odgovor: 8-55%). Zbog toga se preporučuje veća udarna doza kod pacijenata sa AIDS-om. Najveći problem je tahifilaksija (smanjen odgovor organizma na lijek kad se ponovo primjeni nakon kraćeg vremena). Upotreba oktreotida u navedene svrhe još uvijek nije odobrena, odnosno propisuje se *off-label* (upotreba lijeka u neodobrenim dozama, oblicima, putevima primjene, indikacijama), tj. koristi se kao druga linija odbrane. Ukoliko refraktorna dijareja kod pacijenata na hemoterapiji ili sa AIDS-om ne može biti uspješno tretirana loperamidom, može se uključiti oktreotid u dozi 100-500 µg subkutano.

ZAKLJUČCI

Iako se pokazao efikasnim u tretmanu refraktorne dijareje kod pacijenata na hemoterapiji i sa AIDS-om, potrebno je još istraživanja, naročito u kontekstu sigurnosti upotrebe, da bi oktreotid postao registrovan za navedene indikacije.

KLJUČNE RIJEČI: *off-label* upotreba lijekova,oktreotid, refraktorna dijareja, hemoterapija, sindrom stečene imunodeficijencije

USE OF OCTREOTIDE IN THE TREATMENT OF REFRACTORY DIARRHOEA CAUSED BY CHEMOTHERAPY OR ACQUIRED IMMUNODEFICIENCY SYNDROME

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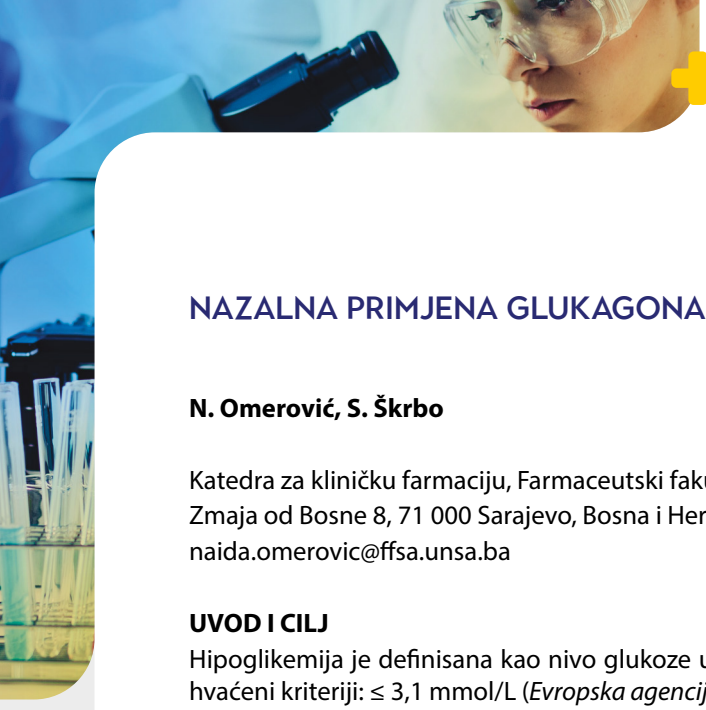
INTRODUCTION AND OBJECTIVE
Octreotide is a synthetic octapeptide and an analogueof endogenous somatostatin, used in the treatment of carcinoids and vasoactive intestinal peptide (*VIP*)-secreting tumors. It blocks the release of various peptides and slows down gastrointestinal motility and intestinal absorption. Refractory diarrhoea lasts longer than 14 days, with no response to the antidiarrhoeals (loperamide) and is most common in patients receiving chemotherapy ordiagnosed with acquired immunodeficiency syndrome (*AIDS*). The objective of this paper is to evaluate the findings of the use of octreotide in the treatment of refractory diarrhoea, its advantages and disadvantages.

METHODS
Systematic research of scholarly and scientific literature, databases (*PubMed*, *Medline*, *EBSCO*, *Science Direct*), electronic journals and books, via general-purpose and specialized search engines (*Google*, *Google Scholar*), using keywords.

RESULTS
In studies investigating the use of octreotide in the treatment of refractory diarrhoea in patients receiving chemotherapy orwith AIDS, doses of 50-5000 µg were administered subcutaneously or intravenously. Its efficacy was evaluated by stool volume and total fluid absorption. It was shown to be more effective in patients receiving chemotherapy (complete response: 86-96%) than in those with AIDS (complete response: 8-55%). A higher initial dose is recommended for patients with AIDS. The biggest problem is tachyphylaxis (decreased response to a drug when re-administered after a short time). The use of octreotide for these purposes has not yet been approved and it is prescribed *off-label* (use of a drug in unapproved doses, forms, routes of administration, indications), so it is used as a second-line treatment. If diarrhoea cannot be successfully treated with loperamide, octreotide may be included, 100-500 µg subcutaneously.

CONCLUSIONS
Although proven effective, more research is needed, especially in the context of safety, so octreotide can be approved in the treatment of refractory diarrhoea in patients receiving chemotherapy orwith AIDS.

KEYWORDS:*off-label*drug use, octreotide, refractory diarrhoea, chemotherapy, acquired immunodeficiency syndrome



NAZALNA PRIMJENA GLUKAGONA U TRETMANU TEŠKE HIPOGLIKEMIJE

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UVOD I CILJ

Hipoglikemija je definisana kao nivo glukoze u krvi niži od referentnog raspona, ali ne postoje općenito prihvaćeni kriteriji: ≤ 3,1 mmol/L (*Evropska agencija za lijekove*); ≤ 3,9 mmol/L (*Američka asocijacija dijabetičara*); ≤ 4,0 mmol/L (*Kanadska asocijacija dijabetičara*). U tretmanu teške hipoglikemije, koja uzrokuje kognitivne poremećaje, pacijenti koriste glukagon intramuskularno. Budući da je intramuskularna primjena bolna, te pacijenti obično trebaju pomoć druge osobe, efikasnost i sigurnost nazalne primjene glukagona je dugo istraživana. Cilj ovog rada je evaluirati saznanja o nazalnoj primjeni glukagona u tretmanu teške hipoglikemije, te prednostima i nedostacima iste.

METODE

Sistemsko pretraživanje stručne i naučne literature, baza podataka (*PubMed*, *Medline*, *EBSCO*, *Science Direct*), elektronskih časopisa i knjiga, preko općih i specijaliziranih pretraživača (*Google*, *Google Scholar*), korištenjem ključnih riječi.

REZULTATI

U studijama u kojima je ispitivana mogućnost nazalne primjene glukagona u tretmanu teške hipoglikemije, korištene su doze 1 - 3 mg nazalno i 1 mg intramuskularno. Njegova efikasnost je procijenjivana na osnovu porasta nivoa glukoze u krvi 15 - 90 minuta nakon primjene. Nivo glukoze u krvi uglavnom se stabilizovao na 6 mmol/L nakon nazalne primjeneglukagona, a kontinuirano se povećavao nakon intramuskularne, do 10 mmol/L. Nije bilo razlike u učestalosti pojavljivanja neželjenih reakcija, osim kihanja, ali se to nije moglo povezati s dozom glukagona, već s vrstom korištenog farmaceutskog oblika. Ispitivane su različite vrste farmaceutskih oblika, ali najperspektivniji su bili inhalatori sa suhim prahom (eng. *Dry-Powder Inhalers*; *DPI*), jer se ovi dozatori za jednokratnu upotrebu mogu čuvati na sobnoj temperaturi, a ni prah ne zahtijeva inhalaciju.

ZAKLJUČCI

Nazalno primijenjeni glukagon odlična je zamjena za intramuskularno primijenjeni glukagon za hitnitretman teške hipoglikemije, posebno za pacijentekoji su već u nesvijesti. Nedavno je *Američka uprava za hranu i lijekove* odobrila prvifarmaceutski oblikza nazalnu primjenu glukagonai nastavit će svoja istraživanja u fazi IV ovog kliničkog ispitivanja.

KLJUČNE RIJEČI: teška hipoglikemija, nazalna primjena lijekova, glukagon

NASAL ADMINISTRATION OF GLUCAGON IN THE TREATMENT OF SEVERE HYPOGLYCAEMIA

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INTRODUCTION AND AIM
Hypoglycaemia is defined as blood glucose level lower than its reference range, but there are no generally accepted criteria: ≤3,1 mmol/L (*European Medicines Agency*); ≤3,9 mmol/L (*American Diabetes Association*); ≤4,0 mmol/L (*Canadian Diabetes Association*). In the treatment of severe hypoglycaemia, which causes cognitive impairments, patients use glucagon intramuscularly. Because intramuscular administration is painful and patients usually require help from another person, efficacy and safety of nasal administration of glucagon was investigated. The objective of this paper is to evaluate the findings of the nasal administration of glucagon in the treatment of severe hypoglycaemia, its advantages and disadvantages.

METHODS
Systematic research of scholarly and scientific literature, databases (*PubMed*, *Medline*, *EBSCO*, *Science Direct*), electronic journals and books, via general-purpose and specialized search engines (*Google*, *Google Scholar*), using keywords.

RESULTS
In studies investigating the nasal administration of glucagon in the treatment of severe hypoglycaemia, doses of 1-3mg were administered nasally and a dose of 1 mg intramuscularly. Its efficacy was evaluated by the increase of blood glucose level 15 - 90 minutes after administration. Blood glucose level was mostly stabilized around 6 mmol/L after nasal administration, but was continuously increasing when administered intramuscularly, up to 10 mmol/L.There was no difference in the occurrence of adverse events, except for sneezing, but this could not be linked to the dose of glucagon but rather to the dosageform. Different dosageforms were investigated, but dry-powder inhalers (*DPI*) were promising, because thesesingle-use dispensers can be stored at the room temperature and powder does not require inhalation.

CONCLUSIONS
Nasally administered glucagon is a great substitution for intramuscularly administered glucagon for emergency treatment of severe hypoglycaemia, especially for unconscious patients. Recently, the *U.S.Food and Drug Administration*approved the first nasal glucagon formulation and will continue with phase IV clinical trial.

KEYWORDS: severehypoglycaemia, nasal drug administration, glucagon

SPECIFIČNOST TERAPIJE HIPERURIKEMIJE FEBUKSOSTATOM U ODNOSU NA KONVENCIONALNO LIJEČENJE ALOPURINOLOM

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UVOD I CILJ

Koncentracija serumske urične kiseline kao potencijalnog markera kardiovaskularnog i cerebrovaskularnog oboljenja i smrtnosti, te glavnog rizikofaktora za razvoj gihta je već 50-ak godina u fokusu medicinskih istraživanja. Rezultati niza studija ukazuju na nedvojbenu djelotvornost febuksostata u bolesnika sa hiperurikemijom i efikasniju učinkovitost u postizanju ciljnog nivoa urične kiseline u odnosu na konvencionalno liječenje alopurinolom. Veza između nivoa urata u serumu i vrijednosti lipida je posebno zanimljiva i donekle oprečna. Uočeno je da visok LDL negativno korelira sa hiperurikemijom, dok je pozitivno koreliranje zabilježeno sa triglyceridima, ukupnim holesterolom i HDL-om. Kako alopurinol, tako i febuksostat pokazuje određeni uticaj na lipidni status.

Cilj rada je pokazati specifičnost terapije hiperurikemije sa febuksostatom i alopurinolom.

METODE

Istraživačkim uzorkom je obuhvaćeno 50 pacijenata, od toga 25 na terapiji febuksostatom, te 25 na terapiji alopurinolom, a odabranih prema definisanim kriterijima.

REZULTATI

Evaluacijom učinkovitosti ispitivanih lijekova na vrijednosti urične kiseline kod hiperurikemičnih pacijenata tretiranih u tromjesečnom i šestomjesečnom periodu, ustanovljeno je da kod pacijenata koji su koristili alopurinol na kraju istraživanja je došlo do smanjenja vrijednosti urične kiseline za 126.28±20.36 µmol/L u odnosu na početnu vrijednost, a kod pacijenata koji su koristili febuksostat na kraju istraživanja je došlo do smanjenja urične kiseline za 252.80±94.17 µmol/L u odnosu na početnu vrijednost. Evaluacijom učinkovitosti alopurinola na vrijednosti triglicerida, uočen je statistički značajan porast vrijednosti triglicerida za 0.33±0.17 mmol/L u odnosu na početnu vrijednost istih, za razliku od grupe koja je koristila terapiju febuksostatom, gdje je uočeno statistički značajno smanjenje za 0.16±0.10 mmol/L.

ZAKLJUČCI

Pacijenti koji su koristili febuksostat imali su niže vrijednosti urične kiseline i niže vrijednosti triglicerida. Iako se alopurinol tokom niza godina upotrebe pokazao kao efikasan lijek u terapiji hiperurikemije, kod pacijenata kod kojih se razvije reakcija preosjetljivosti, ili zbog teške bubrežne insuficijencije im je kontraindiciran ili nedovoljno učinkovit, kao efikasna zamjena se uvodi febuksostat.

KLJUČNE RIJEČI: hiperurikemija, gihт, alopurinol, febuksostat

COMPARISON OF THE EFFECT OF ALLOPURINOL AND FEBUXOSTAT IN HYPERURICEMIC PATIENTS

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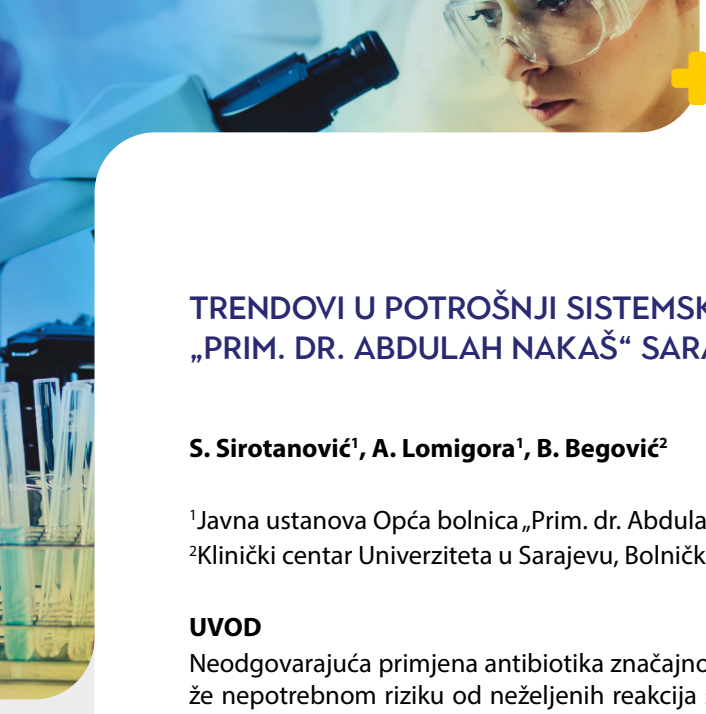
INTRODUCTION AND AIM
Concentration of serum uric acid as a potential marker of cardiovascular and cerebrovascular disease and mortality, and its role in gout development, has been in the focus of medical research and analysis for over 50 years. The correlation between urate levels in serum and lipid values is particularly interesting, but in some studies this correlation is contradictory. Studies have shown that high LDL negatively correlates with hyperuricemia, while positive correlation was observed with triglycerides, total cholesterol and HDL. As allopurinol, febuxostat also show some impact on lipid status. The aim of this study is to show the specificity of the therapy of hyperuricemia with febuxostat and allopurinol.

METHODS
The collection of the material for this work was on a sample of 50 examineess of both genders who were on allopurinol and febuxostat therapy. The inclusion of examineess in the analysis was performed according to defined criterion.

RESULTS
By rating efficiency of examined medicines on values of uric acid on patients with diagnosed hyperuricemia, which were treated in 3- and 6- month period of time, next was established: at the end of research, examinees treated with allopurinol show decrease of uric acid values for 126.28±20.36 μmol/L with regard to beginning values; at the end of research, examinees treated with febuxostat show decrease of uric acid values for 252.80±94.17 μmol/L with regard to beginning values. By rating efficiency of allopurinol on values of triglycerides, at the end of research statistically significant increase was noted. Values of triglycerides were increased for 0.33±0.17 mmol/L with regard to beginning values. By rating efficiency of febuxostat on values of triglycerides, statistically significant decrease for 0.16±0.10 mmol/L was noted.

CONCLUSION
Patients using febuxostat had lower uric acid and lower triglyceride values. Although allopurinol has been shown to be an effective drug in the treatment of hyperuricemia for many years, in patients who develop a hypersensitivity reaction, or due to severe renal failure, is contraindicated or insufficiently effective, febuxostat is introduced as an effective replacement.

KEYWORDS: hyperuricemia, gout, allopurinol, febuxostat



TRENDOVI U POTROŠNJI SISTEMSKIH ANTIBIOTIKA U OPĆOJ BOLNICI „PRIM. DR. ABDULAH NAKAŠ“ SARAJEVO U PERIODU OD 2016 – 2018. GODINE

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UVOD

Neodgovarajuća primjena antibiotika značajno utječe na razvoj rezistencije mikroorganizama i pacijente izlaže nepotrebnom riziku od neželjenih reakcija što povećava ukupnu cijenu liječenja pacijenata u bolničkim i vanbolničkim uslovima.

CILJ

Istražiti trendove potrošnje sistemskih antibiotika u periodu od tri godine u Općoj bolnici „Prim. Dr. Abdulah Nakaš“ Sarajevo (2016 - 2018.). Nakon urađene analize uporediti potrošnju sistemskih antibiotika sa drugim bolnicama u Evropi.

METODE

Analiza potrošnje antibiotika je rađena po metodologiji koju preporučuje WHO (eng. *World Health Organization*), Anatomsko-terapijsko-hemijska (ATC) klasifikacija i definiranim dnevnim dozama (DDD) na broj bolesničkih dana (BD) [1]. U radu su korišteni podaci o potrošnji sistemskih antibiotika u Općoj bolnici „Prim. dr. Abdulah Nakaš“ za period 2016 – 2018. godine kao i broj bolničkih dana za isti period. Lijekovi su prikazani u skladu sa ATC klasifikacijom lijekova WHO i internacionalnim nezaštićenim nazivom (INN) za pojedini lijek.

REZULTATI

Potrošnja sistemskih antibiotika u periodu od tri godine imala je pozitivan trend povećanja (55.67-58.33 DDD/100BD) i zabilježeno je povećanje potrošnje za 5% u periodu od tri godine (2.66-3.18 DDD/100 BD). Sistemski antibiotik koji je najviše propisivan u sve tri godine praćenja je cefalosporin prve generacije cefazolin sa pozitivnim trendom povećanja (16.20-17.28 DDD/100 BD), nešto veća povećanja potrošnje zabilježena su u primjeni klaritromicin tableta (3.29-5.41 DDD/100 BD), metronidazol otopina za infuziju (4.51-4.81 DDD/100 BD) i imipenema sa cilastatinom (0.98-1.61 DDD/100 BD).

ZAKLJUČCI

Analiza potrošnje antibiotika u našoj bolnici pokazala je da je potrošnja antibiotika vrlo slična potrošnji u drugim bolnicama u Evropi.

LITERATURA

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KLJUČNE RIJEČI: anatomsko-terapijsko-hemijska klasifikacija, potrošnja sistemskih antibiotika, definisana dnevna doza

TRENDS IN CONSUMPTION OF SYSTEMIC ANTIBIOTICS AT GENERAL HOSPITAL „PRIM. DR. ABDULAH NAKAS "SARAJEVO IN THE PERIOD FROM 2016 – 2018.

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INTRODUCTION

Inadequate administration of antibiotics significantly affects the development of microbial resistance and exposes patients to the unnecessary risk of adverse reactions, which increases the overall cost of treating patients in hospital and outpatient settings.

OBJECTIVE

Investigate trends in systemic antibiotic consumption over a three-year period at the General Hospital "Prim. Dr. Abdulah Nakas "Sarajevo (2016 - 2018). After the analysis, compare the consumption of systemic antibiotics with other hospitals in Europe.

METHODS

The analysis of antibiotic consumption was performed according to the methodology recommended by the WHO (World Health Organization), Anatomic-Therapeutic-Chemical (ATC) classification and defined daily doses (DDD) on the number of patient days (BD) [1]. The data used for the use of systemic antibiotics at the General Hospital "Prim. dr. Abdulah Nakas "for the period 2016 - 2018 as well as the number of hospital days for the same period. The drugs are presented in accordance with the WHO ATC classification of medicines and the International Non-proprietary Name (INN) for each drug.

RESULTS

Consumption of systemic antibiotics over a three-year period had a positive upward trend (55.67-58.33 DDD/100BD) and a 5% increase in consumption over a three-year period was observed (2.66-3.18 DDD/100 BD). All three years of follow-up is first generation cephalosporin cefazolin with a positive upward trend (16.20-17.28 DDD/100 BD), slightly higher increases in consumption were observed with the use of clarithromycin tablets (3.29-5.41 DDD/100 BD), metronidazole infusion solution (4.51- 4.81 DDD/100 BD) and imipenem with cilastatin (0.98-1.61 DDD/100 BD).

CONCLUSIONS

An analysis of antibiotic consumption at our hospital has shown that antibiotic consumption is very similar to consumption at other hospitals in Europe.

REFERENCES

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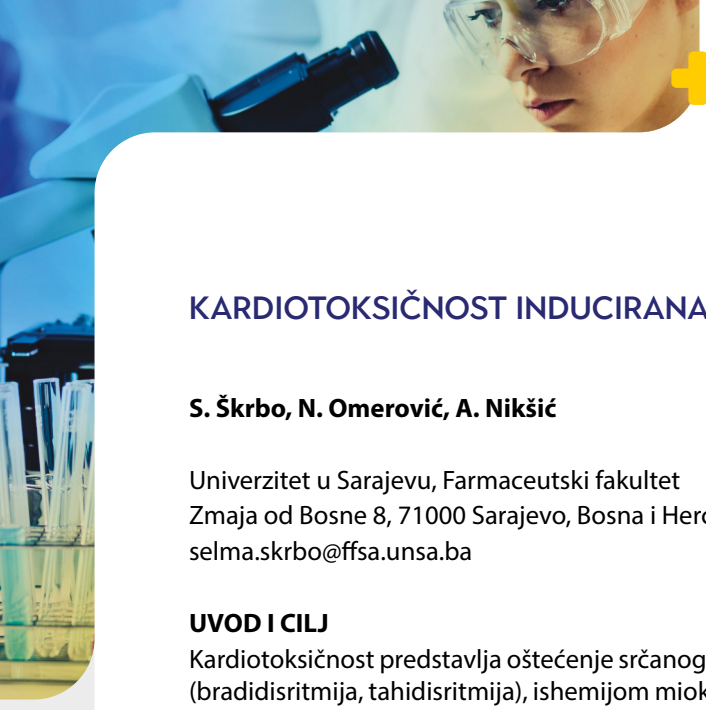
KEY WORDS: anatomical-therapeutic-chemical classification, consumption of systemic antibiotics, defined daily dose



KARDIOTOKSIČNOST INDUCIRANA LIJEKOVIMA

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UVOD I CILJ

Kardiotoksičnost predstavlja oštećenje srčanog mišića, koje se može manifestirati poremećajima srčanog ritma (bradidisritmija, tahidisritmija), ishemijom miokarda, disfunkcijom lijevog ventrikula/srčanom insuficijencijom, miokarditisom, oštećenjem srčanih zalistaka i perikardijalnom bolešću [1]. Gotovo 10% lijekova u posljednje četiri decenije povučeno je sa kliničkog tržišta širom svijeta zbog zabrinutosti za kardiovaskularnu sigurnost [2]. Cilj ovog rada je evaluirati patogenezu različitih oštećenja miokarda uzrokovanih lijekovima, faktore rizika za kardiotoksična oštećenja, te strategije za smanjenje kardiotoksičnih učinaka lijekova.

METODE

Pretraživanje literature vršeno je u bazama podataka *PubMed* i *MEDLINE* upotrebom ključnih riječi: lijek, kardiotoksičnost i oštećenje miokarda.

REZULTATI

Kardiotoksičnost je najčešće inducirana citostaticima, antipsihoticima, antidepresivima, opioidnim analgeticima, nesteroidnim antiinflamatornim lijekovima, lijekovima koji se koriste u tretmanu poremećaja kardiovaskularnog sistema uključujući beta-blokatore, antagoniste kalcija, antagoniste alfa$_1$ i alfa$_2$ receptora i brojnim drugim lijekovima. Kardiotoksičnost može biti primarna i sekundarna, intrinzička i idiosinkrazijska, a mehanizam kardiotoksičnosti inducirane lijekovima je najčešće multifaktorijalan [2, 3]. Manifestacije kardiotoksičnosti ovise o dozi, vrsti i djelovanju lijeka, njegovim farmakokinetičkim karakteristikama, postojećem srčanom oboljenju, genetskim faktorima i dr.

ZAKLJUČCI

Brojni su faktori koji povećavaju osjetljivost pacijenta na kardiotoksičnost lijekova. Sigurna primjena kardiotoksičnih lijekova zahtijeva potpuno razumijevanje predisponirajućih riziko faktora za oštećenje miokarda, uključujući faktore od strane pacijenta i samog lijeka. Praćenje specifičnih srčanih biomarkera može biti značajno za rano otkrivanje, procjenu i monitoring kardiotoksičnosti. Tretman lijekom izazvanog poremećaja miokardijalne funkcije podrazumijeva korekciju doze, istovremenu primjenu antioksidanasa i lijekova za koje se pokazalo da smanjuju kardiotoksičnost izazvanu lijekovima kada se koriste u profilaktičke svrhe ili trenutnu obustavu daljnje primjene suspektnog lijeka te provođenje suportivne terapije.

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[3] Tajiri K, Aonuma K, Sekine I. Cardio-oncology: a multidisciplinary approach for detection, prevention and management of cardiac dysfunction in cancer patients. Japanese Journal of Clinical Oncology. 2017;47(8):678–682.

KLJUČNE RIJEČI: lijek, kardiotoksičnost, oštećenje miokarda

DRUG-INDUCED CARDIOTOXICITY

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INTRODUCTION AND OBJECTIVE

Cardiotoxicity represents damage to the heart muscle which can be manifested as disturbances in cardiac rhythm (bradydysrhythmias, tachydysrhythmias), myocardial ischemia, left ventricular disfunction/heart failure, myocarditis, impairment of cardiac valves and induction of pericardial disease [1]. Almost 10% of drugs in the last four decades have been recalled from the clinical market worldwide due to cardiovascular safety concerns [2]. The purpose of this paper is to review the pathogenesis of different drug-induced myocardial damages, risk factors for cardiotoxic injury, and strategies to decrease the cardiotoxic effects.

METHODS

A literature search was performed in databases of *PubMed* and *MEDLINE* using the keywords: drug, cardiotoxicity, and myocardial injury.

RESULTS

Cardiotoxicity is mostly induced by cytostatics, antipsychotics, opioid analgesics, antidepressants, nonsteroidal anti-inflammatory drugs, drugs used for the treatment of disorders related to the cardiovascular system such as beta-blockers, calcium channel antagonists, $alpha_1$ and $alpha_2$ receptor antagonists and many other drugs. Cardiotoxicity can be primary and secondary, intrinsic and idiosyncratic, and the mechanism of drug-induced cardiotoxicity is usually multifactorial [2, 3]. Manifestations of cardiotoxicity depend on the dose, type and actions of a drug, its pharmacokinetic characteristics, pre-existing cardiac disease, genetic factors, etc.

CONCLUSIONS

There are numerous factors that increase a patient's susceptibility to the cardiotoxicity of drugs. Safe use of cardiotoxic drugs requires a clear understanding of risk factors that predispose to cardiac damage, which include both patient-related characteristics as well as drug-related factors. Measurement of cardio-specific biomarkers can be a valid diagnostic tool for early identification, assessment, and monitoring of cardiotoxicity. Treatment of drug-induced cardiotoxicity consists of the dose regimen correction, concomitant use of antioxidants and drugs which have been shown to reduce drug-induced cardiotoxicity when used in prophylactic setting or immediate withdrawal of suspected drugs and use of supportive therapy.

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[1] Mladěnka P, Applová L, Patočka J, et al. Comprehensive review of cardiovascular toxicity of drugs and related agents. Medical Research Reviews. 2018;38:1332–1403.

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KEYWORDS: drug, cardiotoxicity, myocardial injury

FARMAKOEKONOMSKE MOGUĆNOSTI RACIONALIZACIJE POTROŠNJE LIJEKOVA SA ESENCIJALNE LISTE

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UVOD I CILJ
U Kantonu Sarajevo troškovi lijekova sa esencijalne liste su rasli od 2011. do 2016. godine. Mjerama kontrole potrošnje lijekova i racionalizacijom potrošnje lijekova taj trend rasta potrošnje lijekova je zaustavljen u junu 2016. godine. Cilj ovog rada je ukazati na mogućnosti racionalizacije potrošnje lijekova.

METODE
U ovom radu su korišteni podaci Zavoda zdravstvenog osiguranja Kantona Sarajevo, te metode deskripcije i analize, kao i inovirane smjernice i ograničenja u potrošnji lijekova sa esencijalne liste u Kantonu Sarajevo.

REZULTATI
Cilj "eSmjernice" je da za primjenjive smjernica sa Liste lijekova automatizuje postavljanje ograničenja prilikom propisivanja i/ili izdavanja lijekova, a sastavni je dio informacionog integralnog sistema pod nazivom "EzOblak" Zavoda Zdravstvenog Osiguranja Kantona Sarajevo (ZZOKS). Finansijski efekti primjene "eSmjernice" kroz integralni informacioni sistem se mogu pokazati na primjeru grupe lijekova kao što su nesteroidni antireumatici. Za ovu grupu lijekova inače postoji pisana smjernica ali kontrola ove smjernice nije bila moguća bez primjene alata u integralnom informacionom sistemu odnosno primjene "eSmjernice". Finansijska sredstva izdvojena na mjesečnom nivou za ovu grupu lijekova su iznosila oko 150.000 KM, pa čak i do 175.181 KM u mjesecu martu 2016. godine. Uvođenjem eSmjernica kroz informacioni integralni sistem, potrošnja se uspjela staviti pod kontrolu i potrošnja ove grupe lijekova na mjesečnom nivou je smanjena za oko 100.000 KM i iznosila je oko 45.000 KM. Potrošnja ove grupe lijekova u oktobru 2015. godine je iznosila 147.113 KM, poslije uvođenja eSmjernica potrošnja u oktobru 2016. godine je iznosila 46.651 KM.

ZAKLJUČAK
Zavod je pomoću eSmjernica napravio iskorak i pratio potrošnju po osiguraniku. Ove funkcije su napravljene da pacijent može uzeti tačno onu količinu lijeka koja mu je potrebna na mjesečnom nivou. Poduzete mjere racionalizacije kroz integralni informacioni sistem, su dale rezultat i ostvarene su uštede, koje su pokazane na konkretnom primjeru u ovom radu.

KLJUČNE RIJEČI: farmakoekonomika, eSmjernice, racionalizacija.

PHARMACOECONOMICS POSSIBILITIES FOR RATIONALIZATION OF DRUG'S CONSUMPTION FROM ESSENTIAL LIST

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INTRODUCTION AND OBJECTIVE
In Sarajevo Canton, the costs of essential list of medicine have increased from 2011 to 2016. With measures to control and rationalize drug consumption, this trend of increasing drug consumption was halted in June 2016. The aim of this paper is to point out the possibility of rationalizing drug consumption.

METHODS
This paper uses data from the Health Insurance Institute of the Sarajevo Canton, as well as descriptive and analysis methods, as well as updated guidelines and restrictions on the consumption of medicines from the essential list in the Sarajevo Canton.

RESULTS
The aim of the e-Guideline is to automate the setting of restrictions when prescribing and / or dispensing medicines for the applicable guidelines from the Medicine's List, which is an integral part of the information integral system called "EzCloud" from the Health Insurance Institute of the Sarajevo Canton.
The financial effects of the application of the "e-Guideline" through the integrated information system can be demonstrated on examples of medicines such as non-steroidal anti-rheumatics.
There is a written guideline for this group of medication, but control of this guideline was not possible without the application of tools of the integrated information system or the application of the "e-Guideline".
The financial resources allocated on a monthly basis for this group of medicines amounted to around BAM 150,000 and even up to BAM 175,181 in March 2016.
With the introduction of e-Guidelines through the Integrated Information System, consumption was managed to be controlled and the consumption of this group of medications was reduced by about BAM 100,000 on a monthly basis and amounted to about BAM 45,000. The consumption of this group of medication in October 2015 amounted to BAM 147.113, after the introduction of the e-Guidelines the consumption in October 2016 amounted to BAM 46.651.

CONCLUSION
With the help of the Guidelines, the Institute made a step forward and monitored spending by the insured. These features are designed to allow the patient to take exactly the amount of medicine they need on a monthly basis. The rationalization measures undertaken through the integrated information system have yielded results and savings have been made, which are shown in a concrete example in this paper.

KEYWORDS: pharmacoeconomics, e-Guidelines, rationalization.

ULJE KANABISA: OPRAVDANOST PRIMJENE U TRETMANU MULTIPLE SKLEROZE

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Multipla skleroza (MS) jedna je od najčešćih autoimunih bolesti koja pogađa centralni nervni sistem što rezultira teškim neurološkim oštećenjima. Farmakoterapijski protokol za tretman MS ima za cilj da suprimira progresiju oboljenja što u praksi često rezultira neuspješnim ishodom. U savremenim oblicima liječenje MS sve se više primjenjuju alternativne metode, te nedavne naučne studije ukazuju na opravdanost upotrebe ulja kanabisa čije su aktivne komponente tetrahidrokanabinol (THC) i kanabidiol (CBD). Dosadašnja istraživanja ukazuju na korist primjene ulja kanabisa u palijativnoj njezi, tretmanu neurodegenerativnih oboljenja kao i u tretmanu nekih bolnih stanja. U radu je opisan prikaz slučaja pacijenta, muškarca starosti 20 godina kojem je na osnovu prisustva većeg broja lezija na mozgu dijagnosticirana relaps-remitirajuća forma multiple skleroze a koja se manifestovala u vidu spastičnosti ektremiteta, bolnih napada, gubitka ravnoteže i oslabljenog vida. Imunomodulatorna terapija u trajaju od jedne godine nije rezultirala značajnim poboljšanjem, te se zdravstveno stanje pacijenta pogoršavalo i umanjivalo kvalitet života. Samoincijativnom upotrebom 60 mililitara ulja kanabisa tokom tri mjeseca kod pacijenta je zabilježeno poboljšanje opšteg zdravstvenog stanja, umanjenje bolnih epizoda kao i poboljšanje vida. Najznačajniji pokazatelj efikasnosti tromjesečne terapije uljem kanabisa je smanjenje broja lezija na mozgu detektovanih na kontrolnom snimku magnetne rezonance. Cilj rada je da se ukaže na smanjenje prisutnih simptoma kao i na značajnu razliku između stanja pacijenta prije i poslije korištenja ulja kanabisa u tretmanu MS. Prikazanim rezultatima se potvrđuju dosadašnja saznanja o upotrebi ulja kanabisa što inicira potrebu za razmatranjem legalizacije kanabisa u medicinske svrhe u Bosni i Hercegovini.

KLJUČNE RIJEČI: ulje kanabisa, multipla skleroza, lezije

CANNABIS OIL: POSSIBILITY OF APPLICATION IN TREATMENT OF MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is one of the most common autoimmune disorders which effects central nervous system and results with severe neurological defects. Aim of pharmacotherapy protocol for treatment of MS is to suppress progression of disease which often results with unsuccessful outcome. In today's MS forms of treatment alternative methods are becoming more applicable and recent studies have justified usage of cannabis oil whose active compounds are tetrahydrocannabinol (THC) and cannabidiol (CBD). Recent studies demonstrated benefit of applying cannabis oil in palliative care, treatment of neurodegenerative diseases and different forms of pain management. This paper describes case report of 20-year-old male patient with diagnosed relapsing-remitting multiple sclerosis based on number of detected brain lesions which manifested with spasm of muscles, loss of balance, various painful conditions and weaken eyesight. One year long immunomodulatory therapy resulted with deterioration of general health status and reduction of quality of life. After three months long treatment with self-administrated 60 ml of cannabis oil general health status of patient has been improved significantly. Furthermore, reduction of pain conditions and improvement of eyesight was noted. The most important indicator of efficiency of applied cannabis oil therapy was reduction in number of lesions detected on control scans of brain. The aim of this paper is to compare differences in patient's condition before and after cannabis oil application in treatment of MS and to outline the reduction of noted symptoms. Findings of this study justified former knowledge and recent studies about application of cannabis oil in treatment of MS which indicated the need to consider legalization of cannabis in medical purposes in Bosnia and Herzegovina.

KEY WORDS: cannabis oil, multiple sclerosis, lesions.

FARMAKOGNOZIJA I FITOTERAPIJA

UVODNO PREDAVANJE

FITOEKVIVALENTNOST: PREDUSLOVI ZA KORIŠTENJE KLINIČKIH PODATAKA KOD BILJNIH LIJEKOVA

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UVOD I CILJ

Ključno za marketinšku autorizaciju biljnih lijekova su dokazi o efikasnosti i bezbjednosti. To se može postići na različite načine: na osnovu potpunog dosijea sa vlastitim studijama o efikasnosti i bezbjednosti, mješovitog dosijea ili bibliografskog dosijea. Pored toga, sigurnost i efikasnost tradicionalnih biljnih lijekova dokazana je dugom tradicionalnom upotrebom.

Svrha ovog rada bila je diskusija o specifičnostima odobravanja odnosno registracije biljnih lijekova, o problemima koji se mogu pojaviti kod analitičkog poređenja biljnih ekstrakata, te da se istraže detalji biljnih preparata u publikacijama kliničkih ispitivanja.

METODA

Metoda koja se koristila za odgovaranje na pitanja u ovom radu ograničena je na pretraživanje literature u bazama podataka, informacije sa web stranice Evropske agencije za lijekove, udžbenike i časopise (uključujući i online verzije).

REZULTATI

Posebno kada je u pitanju bibliografski dosije, bitno je kako se može dokazati ekvivalentnost primijenjenog proizvoda u skladu s proizvodima koji su korišteni u kliničkim ispitivanjima. Monografije Evropske unije pružaju veoma dobru pomoć za podnosioca zahtjeva. Međutim, samo u slučaju standardizovanih ekstrakata, u kojima su definisane supstance odgovorne za kliničku efikasnost, može se govoriti o istim aktivnim supstancama. Za većinu "drugih" ekstrakata, supstance odgovorne za efikasnost nisu poznate. Da bi se bolje karakterizirali klinički testirani ekstrakti, potrebno je provesti istraživanje u kliničkoj oblasti. Nažalost, nauka je trenutno ograničena uglavnom na prekliničke aspekte.

Osnovni problem kliničkih istraživanja sa biljnim lijekovima je da ne postoji zaštita podataka za poznate aktivne supstance. Ovo bi se odnosilo samo na nove ekstrakte, koji bi, prema trenutnim smjernicama, trebali biti razvijeni sa sveobuhvatnim prekliničkim i kliničkim podacima.

ZAKLJUČCI

Općenito, poticaji za klinička istraživanja biljnih preparata gotovo da i ne postoje. Kako bi se nastavilo sa održavanjem visokokvalitetnih biljnih lijekova na tržištu, zakonodavac je posebno pozvan da stvori povoljan okvir i da preispita trenutno vrlo atraktivne, ali nedovoljno regulirane kanale distribucije (na primjer, za dodatke prehrani).

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KLJUČNE RIJEČI: fitoekvivalentnost, biljni lijekovi, marketinška autorizacija, dobro utvrđena upotreba, tradicionalna upotreba

PHYTOEQUIVALENCE: REQUIREMENTS FOR REFERENCE TO CLINICAL DATA IN HERBAL MEDICINAL PRODUCTS

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INTRODUCTION AND OBJECTIVE

Crucial for a marketing authorisation of herbal medicinal products are evidence of efficacy and safety. This can be done in different ways: on the basis of a full dossier with proprietary efficacy and safety studies, a mixed dossier or a bibliographic dossier. In addition, the safety and efficacy of traditional herbal medicines is proven by their long traditional use.

The purpose of this work was to discuss the specificities of the authorization respectively registration of herbal medicinal products, to discuss problems that may arise in the analytical comparison of herbal extracts and to investigate the details of the herbal preparations in the publications of the clinical trials.

METHODS

The method used to answer the questions in this work is limited to literature searches in databases, information from the website of the European Medicines Agency, textbooks and journals (including online versions).

RESULTS

Particularly for bibliographic applications for marketing authorisation the question is essential, how the equivalence of the applied product can be demonstrated in accordance with products, which were used in the clinical trials. The EU-Monographs of HMPC provide a very good assistance for an applicant. However, only in the case of standardized extracts, in which defined constituents are responsible for clinical efficacy, can be spoken of the same active ingredients. For the most "other" extracts, the constituents responsible for the efficacy are not known. In order to better characterize the clinically tested extracts, research into clinical field would be required. Unfortunately, it is currently limited mainly to preclinical aspects.

The fundamental problem of clinical research with herbal medicines is that there is no data protection for known active substances. This would only apply to novel extracts, which, according to the current guidelines, would need to be developed with comprehensive preclinical and clinical data.

CONCLUSIONS

Altogether, the incentives for clinical research of herbal preparations are almost non-existent. In order to continue to keep high-quality herbal medicines on the market, the legislator in particular is called upon to create a conducive framework and to rethink the currently very attractive but under-regulated distribution channels (for example, for food supplements).

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KEY WORDS: phytoequivalency, herbal medicinal products, marketing authorization, well-established use, traditional use

UVODNO PREDAVANJE

NUTRITIVNI I BIOAKTIVNI SASTOJCI ODABRANIH GLJIVA IZ FAMILIJA POLYPORACEAE, CANTHARELLACEAE I LYOPHYLLACEAE

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UVOD I CILJ

Jestive gljive su važan izvor hranljivih i bioaktivnih jedinjenja sa različitim farmakološkim aktivnostima. Ekstrakti gljiva *Fomes fomentarius-FF, Laetiporus sulphureus-LS, Cantarellus cibarius-CC, Cratherellus cornucopioides-CrC i Calocibe gambosa-CG* bile su predmet hemijske analize i *in vitro* ispitivanja nekoliko aktivnosti: antioksidantne, citotoksične, antibakterijske i ACE inhibitorne aktivnosti.

METODE

Korišćene su različite metode: nutritivna vrednost - AOAC metode; sadržaj masnih kiselina - GC-FID-MS; aminokiseline - LC-MS; nukleotidi - HPLC; ukupni polifenoli i sadržaj β-glukana - spektrofotometrija; ukupna vlakna - gravimetrija; mikro- i makroelementi - atomska emisiona spektrometrija; antioksidativna aktivnost - DPPH test; antimikrobna aktivnost - agar dilucioni test; citotoksičnost - MTT test; ACE inhibitorna aktivnost - komercijalni enzimski test).

REZULTATI

Sve gljive su imale nisku energetsku vrednost i sadržaj masnih kiselina, ali su bile bogate vlaknima i β-glukanima. Najzastupljeniji elementi su Ca, zatim K i P, a odnos Na/K je bio veoma povoljan. S druge strane, Pb, As i Cd su detektovani u većoj količini od dozvoljene. Analizirane gljive, posmatrajući sadržaj nukleotida, nalaze se u grupi gljiva sa umerenim sadržajem nukleotida. *CG* i *CrC* sadrže esencijalne i ne-esencijalne aminokiseline. Postoji korelacija između ukupnog sadržaja fenola i sposobnosti uklanjanja DPPH radikala. Testirane gljive (*FF*, *LS*, *CC*, *CrC*) su imale umerenu antibakterijsku aktivnost protiv odabranih bakterijskih sojeva, osim protiv *H. pilori* gde su vrednosti MIC bile veoma niske (MIC između 4 i 32 mg/mL). Takođe, citotoksičnost testiranih gljiva bila je značajna prema HeLa i N87 ćelijskim linijama, sa različitom aktivnošću protiv linije zdravih ćelija MRC5. ACE inhibitorna aktivnost vodenih ekstrakata *CC*, *CrC* i *FF* bila je značajna [1,2,3].

ZAKLJUČCI

Veoma obećavajući rezultati sugerišu da određeni ekstrakti gljiva mogu biti korisni u smanjenju simptoma metaboličkog sindroma, ali i u anti-tumorskoj terapiji.

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KLJUČNE RIJEČI: *Fomes fomentarius, Laetiporus sulphureus, Cantahrellus cibarius, Cratherellus cornucopioides, Calocybe gambosa*

NUTRITIONAL AND BIOACTIVE INGREDIENTS OF SELECTED MUSHROOMS FROM FAMILIES POLYPORACEAE, CANTHARELLACEAE AND LYOPHYLLACEAE

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INTRODUCTION AND OBJECTIVE

The edible mushrooms are important source of nutritive and bioactive compounds with different pharmacological activities. Extracts of fungi *Fomes fomentarius-FF*, *Laetiporus sulphureus-LS*, *Cantarellus cibarius-CC*, *Cratherellus cornucopioides-CrC* and *Calocybe gambosa-CG*, were the subject of chemical analysis and *in vitro* testing of several activities: antioxidant, cytotoxic, antibacterial activity, ACE inhibitory activity.

METHODS

Different methods were used: nutritional value - AOAC methods; content of fatty acids - GC-FID-MS method; amino acids - LC-MS; nucleotides - HPLC; total polyphenols and β-glucan content - spectrophotometry; total fibers - gravimetric method; micro- and macroelements - atomic emission spectrometry; antioxidant activity - DPPH test; antimicrobial activity - agar dilution test; cytotoxicity - MTT test; ACE inhibitory activity - commercial enzyme test).

RESULTS

All fungi had low energy values and the content of fatty acids, but they are rich in total fibers and β-glucan content. The most abundant elements were Ca, followed with K and P, and with very favorable Na/K ratio. On the other hand, Pb, As and Cd were detected in level higher than allowed. Analyzed fungi, concerning the content of nucleotides, are in the group of fungi with moderate level of nucleotides. *CG* and *CrC* contained essential and non-essential amino acids. There was the correlation between total phenolic content and anti-DPPH radical scavenging activity. The tested fungi (*FF, LS, CC, CrC*) possessed moderate antibacterial activity against selected bacterial strains, except against *H. pylori* where MIC values were very low (MIC between 4 and 32 μg/mL). In addition, cytotoxicity of tested fungi was significant against HeLa and N87 cell lines, with different activity against healthy MRC5 cell line. ACE inhibitory activity of aqueous extract of *CC*, *CrC* and *FF* was significant [1,2,3].

CONCLUSIONS

Very promising results suggested that certain mushroom extracts could be beneficial in reducing symptoms of metabolic syndrome, but also in anti-tumor therapy.

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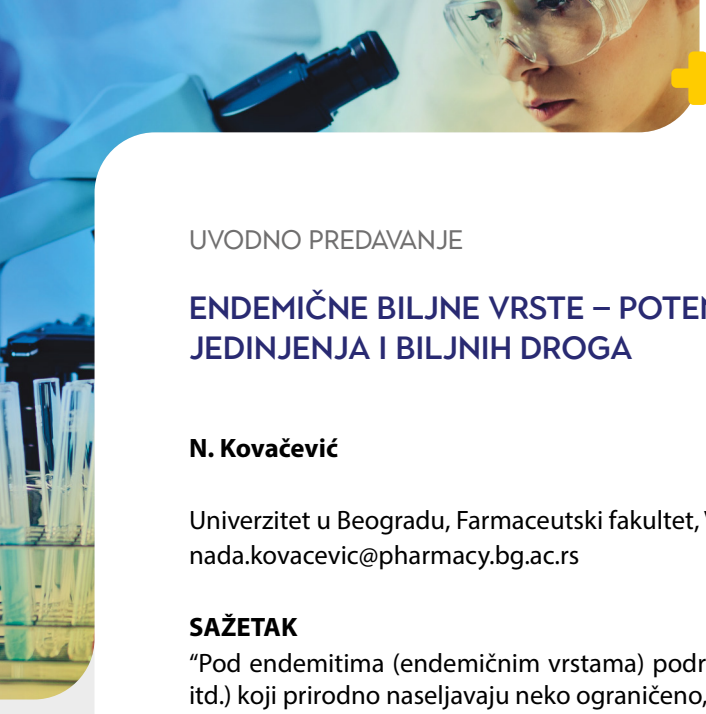
KEY WORDS: *Fomes fomentarius, Laetiporus sulphureus, Cantahrellus cibarius, Cratherellus cornucopioides, Calocybe gambosa*



UVODNO PREDAVANJE

ENDEMIČNE BILJNE VRSTE – POTENCIJALNI IZVOR NOVIH PRIRODNIH JEDINJENJA I BILJNIH DROGA

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SAŽETAK

"Pod endemitima (endemičnim vrstama) podrazumevamo žive stisteme (populacije, podvrste, vrste, rodove itd.) koji prirodno naseljavaju neko ograničeno, veće ili manje, geografsko područje, nasuprot kozmopolitskim vrstama, koje su široko rasprostranjene gotovo po čitavoj zemljinoj površini. Današnja rasprostranjenost biljaka nije uslovljena samo ekološkim prilikama nekog područja, već je i posledica njihove geološke prošlosti." [1]

Uslovi za pojavu endemizma među biljkama, najčešće, jesu geografske, ekološke ili genetičke prirode. Sve navedeno može uticati i na fiziološke i metaboličke procese u biljkama, pa i na produkte ovih procesa. Sekundarni metaboliti biljaka sigurno su delom uključeni u adaptaciju i preživljavanje biljnih vrsta na određenom životnom staništu. Sa druge strane, sekundarni metaboliti biljaka su uvek interesantan objekat za istraživače prirodnih lekovitih sirovina. Za njih su endemične biljke interesantne zbog najmanje dve činjenice: zato što nisu široko dostupne istraživačima i zbog potencijalne specifičnosti metaboličkih procesa i mogućnosti otkrivanja novih biološki/farmakološki aktivnih metabolita.

I pored kombinatorne hemije i postojanja mogućnosti za kompjutersko dizajniranje lekova, prirodna jedinjenja definisane biološke/farmakološke aktivnosti i dalje predstavljaju veoma značajne modele za sintezu efikasnijih i bezbednijih lekova. Nove hemijske strukture i modeli naročito su značajni u oblasti antibitika, antiinfamatornih i lekova za terapiju malignih oboljenja, kao i supstanci koje mogu uticati na prevenciju i terapiju različitih oblika neurodegenerativnih bolesti.

U predavanju će biti komentarisani primeri važnijih prirodnih jedinjenja i endemične biljne vrste iz kojih su ona izolovana. Takođe, biće predstavljena lična istraživanja koja su povezana sa endemičnim biljkama Balkana. Najčešće su ispitivane vrste iz aromatičnih rodova (*Pinus, Achillea, Seseli, Satureja*), a pored analize etarskih ulja rađena je intra- i interspecijska hemijska analiza (*Valeriana* spp.), kao i skrining određenih farmakoloških aktivnosti (*Achillea alexandri-regis, Seseli gracile* …).

Inače, podaci govore da u flori Republike Srbije postoji 287 endemita, dok područje Balkana ima ukupno 6750 biljnih vrsta od kojih je 2600 endemično. Poznato je da je područje Balkana jedan od svetskih centara biodiverziteta i endemizma. [2] Zbog toga, vodeći računa o zaštiti i očuvanju biodiverziteta, istraživači iz ovog regiona posvećeni su proučavaju njegovih potencijale i različitih mogućnosti korišćenja.

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KLJUČNE RIJEČI: endemične biljne vrste, klasifikacija, sekundarni metaboliti, hemijska analiza, farmakološki skrining

ENDEMIC PLANT SPECIES – POTENTIAL SOURCE OF NEW NATURAL SUBSTANCES AND HERBAL DRUGS

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SUMMARY

"By endemics (endemic species) we mean living systems (populations, subspecies, species, genera, etc.) that naturally inhabit a limited, larger or smaller geographical area, as opposed to cosmopolitan species, which are widespread almost throughout the earth. The current distribution of plants is not only conditioned by the environmental conditions of an area, but is also a consequence of their geological past. "[1]

Conditions for endemism among plants, most often, are geographical, ecological or genetic in nature. All of the above can affect the physiological and metabolic processes in plants, as well as the products of these processes. Secondary plant metabolites are certainly partly involved in the adaptation and survival of plant species in a particular habitat. On the other hand, secondary metabolites of plants are always an interesting object for researchers of natural medicinal raw materials. Endemic plants are of interest to them because of at least two facts: because they are not widely available to researchers and because of the potential specificity of metabolic processes and the ability to dicover new biologically / pharmacologically active metabolites.

Despite the combinatorial chemistry and the possibility of computer-aided drug design, natural compounds of defined biological / pharmacological activity still represent very significant models for the synthesis of more effective and safe drugs. New chemical structures and models are particularly important in the fields of antibiotics, anti-inflammatory and drugs for the treatment of malignancies, as well as substances that can influence the prevention and therapy of various forms of neurodegenerative diseases.

Examples of important natural compounds and endemic plant species from which they are isolated will be discussed in the lecture. Also, personal research related to the endemic plants of the Balkans will be presented. Species from aromatic genera (*Pinus, Achillea, Seseli, Satureja*) were most commonly examined, and in addition to the analysis of essential oils, intra- and interspecific chemical analysis (*Valeriana* spp.) was performed, as well as screening for certain pharmacological activities (*Achillaea alexandri-regis*, *Seseli gracile*…). Otherwise, the data indicate that there are 287 endemics in the flora of the Republic of Serbia, while in the Balkans there are a total of 6750 plant species, of which 2600 are endemic. The Balkan area is known to be one of the world's centers of biodiversity and endemism. [2] Therefore, taking into account the protection and conservation of biodiversity, researchers from this region are committed to exploring its potential and its various uses.

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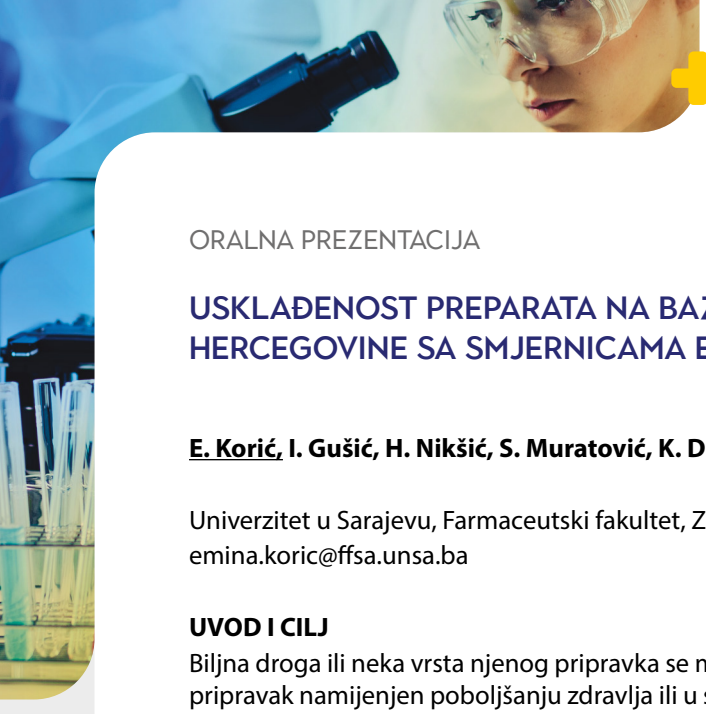
KEY WORDS: endemic plant species, classification, secondary metabolites, chemical analysis, pharmacological screening



ORALNA PREZENTACIJA

USKLAĐENOST PREPARATA NA BAZI *VALERIANA OFFICINALIS* NA TRŽIŠTU BOSNE I HERCEGOVINE SA SMJERNICAMA EUROPSKE AGENCIJE ZA LIJEKOVE

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UVOD I CILJ

Biljna droga ili neka vrsta njenog pripravka se može pojaviti na tržištu paralelno kao lijek, kao hrana i kao biljni pripravak namijenjen poboljšanju zdravlja ili u svrhu kozmetike [1]. U ovom radu evaluirali smo parametre koji se prate kao kriterij izrade preparata na bazi *Valeriana officinalis* baziranih na naučnim dokazima i tradicionalnoj upotrebi.

METODE

Dostupne monografije Komiteta za herbalne lijekove pri Europskoj agenciji za lijekove (engl. *European Medicines Agency*, EMA) za drogu Valerianae radix korišteni su kao izvor informacija za poređenje parametara kriterija izrade fitopreparata. Pravilnost izrade i deklaracije 12 fitopreparata različitog regulatornog statusa na tržištu Bosne i Hercegovine evaluiran je na osnovu sljedećih parametara: upotreba adekvatne biljne droge, odabir adekvatnog pripravka biljne droge, odnos droge i otapala, adekvatan odabir otapala, doziranje i preporuke režima doziranja.

REZULTATI

Ukupno pet analiziranih fitopreparata na bazi *Valeriana officinalis* imaju status lijeka na tržištu Bosne i Hercegovine koji ispunjavaju sve parametre kriterija od strane EMA za stavljanje lijeka u promet zasnovanih na naučnim dokazima. Samo jedan analizirani fitopreparat na bazi *Valeriana officinalis* ima status tradicionalnog biljnog lijeka na tržištu Bosne i Hercegovine koji ispunjava sve parametre kriterija od strane EMA za stavljanje lijeka u promet zasnovanog na tradicionalnoj upotrebi. Šest analiziranih fitopreparata na bazi *Valeriana officinalis* ima status dijetetskog suplementa u okviru kojih se uočavaju značajna odstupanja od smjernica za deklaraciju biljne droge i biljnog pripravka u biljnom lijeku ili tradicionalnom biljnom lijeku.

ZAKLJUČCI

Dostupne monografije EMA su trenutno adekvatni kriteriji za stavljanje u promet samo za biljne lijekove i / ili tradicionalne biljne lijekove, dok u Europskoj uniji još nije odlučeno na koji će se način provesti evaluacije zdravstvenih tvrdnji biljnih vrsta u odnosu na dodatke prehrani, stoga nepravilnosti precizno definisanih parametara izrade i deklaracije samog proizvoda jesu posljedica nedovoljno definisanih nacionalnih legislativa kao i kontrole tržišta dijetetskih suplemenata.

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KLJUČNE RIJEČI: fitopreparati, biljni lijek, dijetetski suplement, *Valeriana officinalis*

COMPLIANCE OF *VALERIANA OFFICINALIS* PHYTOPREPARATIONS ON THE MARKET OF BOSNIA AND HERZEGOVINA WITH EUROPEAN MEDICINE AGENCY GUIDELINES

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INTRODUCTION AND OBJECTIVE
A herbal drug or its preparation may appear on the market in parallel as a medicine, as a food and as a herbal preparation intended for health or cosmetic purposes [1]. The criteria for the manufacturing the *Valeriana officinalis* phytopreparations based on scientific evidence and traditional use were evaluated in this paper.

METHODS
The European Medicines Agency (EMA) monographs for the drug Valerianae radix were used as a source of information to compare the design criteria of the avaliable phytopreparations. The 12 phytopreparations with different regulatory status on the market of Bosnia and Herzegovina has been evaluated regarding the correctness of their manufacturing and declaration on the basis of the following parametars: use of an adequate herbal drug, selection of the adequate herbal drug preparation, drug-solvent ration, adequate solvent selection, dosage and dosage regimen recommendations.

RESULTS
A total of five *Valeriana officinalis* phytopreparations have the status of a medicinal product on the market of Bosnia and Herzegovina, which fulfills all the parameters of the EMA criteria for placing a medicinal product on the market based on scientific evidence. Only one *Valeriana officinalis* phytopreparation has the status of traditional herbal medicinal product on the market of Bosnia and Herzegovina, which fulfills all the parameters of the EMA criteria for placing a medicinal product on the market based on traditional use. The six *Valeriana officinalis* phytopreparations have status as dietary supplement, within which significiant deviations from the EMA recomendend guidelines for the declaration of a herbal drug and herbal preparation in phytopreparations are observed.

CONCLUSIONS
The available EMA monographs are currently adequate criteria only for herbal medicinal and/or traditional herbal medicinal product, whereas it has not yet been decided in the European Union how evaluations of plant health claims in dietary supplements will be conducted. Therefore, irregularities of the well-defined parameters of production and declaration of the analyzed phytopreparations are the result of insufficiently defined national legislation and control of the dietary supplement market.

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KLJUČNE RIJEČI: phytopreparation, herbal medicinal product, dietary supplement, *Valeriana officinalis*

ORALNA PREZENTACIJA

USKLAĐENOST PREPARATA NA BAZI ANTRAHINONSKIH GLIKOZIDA NA TRŽIŠTU BOSNE I HERCEGOVINE SA SMJERNICAMA EUROPSKE AGENCIJE ZA LIJEKOVE

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UVOD I CILJ

Ujednačenost fitohemijskog sastava, te kvalitet biljnih droga i ekstrakata koji se koriste kao polazna sirovina za proizvodnju ljekovitih preparata na bazi antrahinonskih glikozida preduvjet su ostvarivanju njihove sigurne i učinkovite primjene. S obzirom na popularnost u samoliječenju, te postojanje značajne razlike u regulatornim zahtjevima komercijalnih pripravaka u statusu lijeka ili dodatka prehrani na tržištu Bosne i Hercegovine (BiH), cilj istraživanja bio je utvrditi usklađenost izrade i deklaracije dostupnih fitopreparata na bazi antrahinonskih glikozida sa smjernicama Europske agencije za lijekove (engl. *European Medicines Agency*, EMA).

METODE

Istraživanjem je obuhvaćeno 15 fitopreparata na bazi antrahinonskih glikozida koji se prometuju u apotekama i/ili biljnim apotekama na području BiH. Evaluirana je opravdanost statusa fitopreparata kao lijeka ili dodatka prehrani na osnovu poređenja sljedećih kriterija sa smjernicama EMA: upotreba adekvatne biljne droge i/ili njenog pripravka za terapijsku indikaciju opstipacija, farmaceutski oblik, tačno definiran sastav proizvoda i sadržaj aktivnih principa, doziranje i način upotrebe naveden od strane proizvođača,

REZULTATI

Ukupno pet preparata na bazi antrahinonskih glikozida ima status lijeka na tržištu BiH i ispunjavaju sve smjernice navedene u EMA monografijama droga. Samo jedan od ukupno deset uzoraka registriranih kao dodatak prehrani sadrži standardizirani suhi ekstrakt droge sa navedenim udjelom antrahinonskih spojeva. U devet od deset uzoraka nije naveden udio antrahinonskih glikozida u pojedinačnoj dozi. Neadekvatnost prilikom izražavanja sastava preparata i/ili režima doziranja u pogledu prekoračenja maksimalnih dnevnih doza antrahinonskoih glikozida uočena je kod svih 10 analiziranih preparata registriranih kao dodatak prehrani.

ZAKLJUČCI

S obzirom na značajna odstupanja deklaracije sastava i režima doziranja analiziranih fitopreparata registriranih kao dodatak prehrani u odnosu na biljne lijekove, neophodno je provesti njihovu kvalitativnu i kvantitativnu analizu u cilju provjere zahtjeva monografija za sadržaj aktivnih principa. Ističe se potreba za unaprijeđenjem legislative BiH u području dodatnih ograničenja i upozorenja za biljne vrste koje se mogu koristiti u proizvodnji dodataka prehrani.

KLJUČNE RIJEČI: fitopreparati, biljni lijek, dodatak prehrani, antrahinonski glikozidi

COMPLIANCE OF ANTHRAQUINON GLYCOSID BASED PRODUCTS ON THE MARKET OF BOSNIA AND HERZEGOVINA WITH THE EUROPEAN MEDICINE AGENCY GUIDELINES

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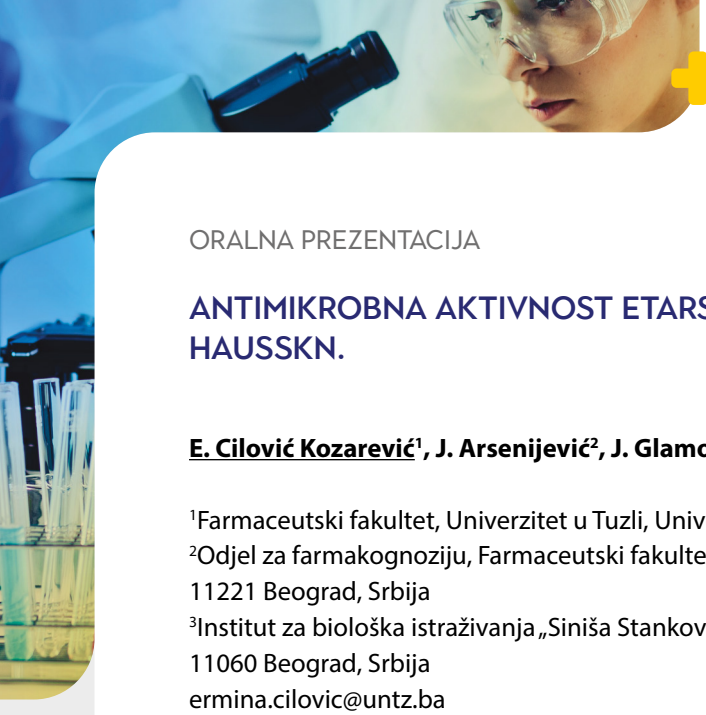
INTRODUCTION AND OBJECTIVE
The uniformity of the phytochemical composition and the quality of herbal drugs and extracts used as a starting material for the production of anthraquinone glycoside-based medicinal preparations are prerequisites for their safe and effective application. The aim of the study was to determine the compliance of the anthraquinone glycosides based phytopreparations with European Medicines Agency (EMA) guidelines due to the popularity of self-medication and the significant difference in regulatory requirements for commercial preparations in the status of a medicinal product or dietary supplement on the market of Bosnia and Herzegovina (BiH).

METHODS
The study included 15 phytopreparations based on anthraquinone glycosides sold in pharmacies and/or herbal pharmacies in BiH. The justification of the phytopreparations status as a medicine or dietary supplement was evaluated on the basis of a comparison of the following criteria with the EMA guidelines: use of an adequate herbal drug and/or its preparation for therapeutic indication of constipation, pharmaceutical form, well-defined product composition and active principle content, dosage and dosage regimen recommendations stated by the manufacturer.

RESULTS
A total of five anthraquinone glycoside preparations have the status of a drug on the BiH market and fulfill all the guidelines stated in the EMA drug monographs. Only one out of ten samples registered as a dietary supplement contains a standardized dry drug extract with the indicated content of anthraquinone compounds. Nine out of ten samples did not indicate the proportion of anthraquinone glycosides in a single dose. Inadequacy in expressing the composition of the preparations and/or dosage regimen with respect to exceeding the maximum daily doses of anthraquinone glycosides was observed in all 10 analyzed preparations registered as a dietary supplement.

CONCLUSIONS
The significant variations in the composition and dosage declaration of the analyzed phytopreparations registered as a dietary supplement in relation to herbal medicines were observed. It is necessary to carry out their qualitative and quantitative analysis in order to verify the requirements of the monographs for the content of the active principles. The need to improve BiH legislation in the area of additional restrictions and warnings for plant species that can be used in the production of nutritional supplements is emphasized.

KEY WORDS: phytopreparations, herbal medicine, dietary supplement, anthraquinone glycosides



ORALNA PREZENTACIJA

ANTIMIKROBNA AKTIVNOST ETARSKOG ULJA *INULAE VERBASCIFOLIAE* (WILD.) HAUSSKN.

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UVOD I CILJEVI: *Inula verbascifolia* (Willd.) Hausskn., Asteraceae je rasprostranjena od istočne obale Italije, duž dalmatinske obale, jugoistoka Balkana i Krete do Male Azije, Pontusa i Sirije [1]. Dosadašnja fitohemijska istraživanja ove biljne vrste se pretežno odnose na sastav etarskog ulja nadzemnih dijelova sa područja Grčke, Italije i Hrvatske. Cilj rada je odrediti sastav etarskog ulja nadzemnih dijelova *I. verbascifolia* sakupljene za vrijeme cvjetanja biljke na području Mostara, Bosna i Hercegovina, te ispitati njegovu antimikrobnu aktivnost.

METODE: Kvalitativna i kvantitativna analiza sastavnih komponenata etarskog ulja je izvedena primjenom gasne hromatografije i gasne hromatografije - masene spektrometrije (GC i GC-MS) [2]. Ispitivanje antimikrobne aktivnosti etarskog ulja je urađeno na šest bakterijskih vrsta i na *Candida albicans* u *in vitro* uslovima mikrodilucionom metodom [3].

REZULTATI: Sadržaj etarskog ulja herbe *I. verbascifoliae* je iznosio 0,01%. Identifikovano je 17 komponenata što je predstavljalo 86,95% ukupnog sastava ulja. Dominantne komponente su bile *α*-murolol (14,82%), tridekanal (10,19%), (*3Z*)- heksenil benzoat (8,20%), nonakozan (7,11%), linalol (5,55%), *α*-kadinol (5,36%) i undekanal (5,22%). Etarsko ulje je inhibiralo rast gram-pozitivnih i gram-negativnih testiranih bakterija i pokazalo najmanju minimalnu inhibitornu koncentraciju protiv kliničkih sojeva *Staphylococcus aureus* i *Bacillus cereus.*

ZAKLJUČCI: Komponente etarskog ulja nadzemnih dijelova *I. verbascifoliae* sa područja Bosne i Hercegovine u poređenju sa do sada objavljenim rezultatima se razlikuju. Antibakterijski esej koji se odnosi na pomenuto etarsko ulje je pokazao antibakterijsku aktivnost. To može pomoći u identifikaciji i razvoju novih efektivnih antimikrobnih agenasa. Dalje analize za prečišćavanje i karakterizaciju aktivnih komponenti su potrebne.

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KLJUČNE RIJEČI: *Inula verbascifolia*, nadzemni dijelovi, etarsko ulje, antimikrobna aktivnost.

ANTIMICROBIAL ACTIVITY OF *INULA VERBASCIFOLIA* (WILD.) HAUSSKN. ESSENTIAL OIL

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INTRODUCTION AND OBJECTIVE: *Inula verbascifolia* (Willd.) Hausskn., Asteraceae is distributed from the East coast of Italy through the Dalmatian coastline, southern Balkans and Crete to Asia Minor, Pontus and Syria [1]. So far, phytochemical investigations of this plant species are mainly related to the composition of the aerial parts essential oil from the areas of Greece, Italy and Croatia. The aim of this work was to determine the composition of the essential oils of *I. verbascifolia* aerial parts collected during flowering time of the plant in the area of Mostar, Bosnia and Herzegovina, and to examine its antimicrobial activity.

METHODS: Qualitative and quantitative analyze of constituent components of essential oil was performed using gass chromatography and gass chromatography-mass spectrophotometry (GC and GC-MS) [2]. The assay of the antimicrobial activity of the essential oil was performed on six bacterial strains and on *Candida albicans in vitro* by a microdilution method [3].

RESULTS: The content of the essential oil of the *I. verbascifolia* aerial parts was 0.01%. 17 components were identified which represented 86.95% of the total oil composition. The major oil constituents were found to be *α*-murolol (14.82%), tridecanal (10.19%), (3*Z*)-hexenyl benzoate (8.20%), nonacosane (7.11%), linalol (5.55%), *α*-cadinol (5.36%) and undecanal (5.22%). The essential oil inhibited the growth of gram-positive and gram-negative tested bacteria and presented the lowest minimal inhibitory concentration against clinical strains of *Staphylococcus aureus* and *Bacillus cereus.*

CONCLUSIONS: The components of the essential oil of *I. verbascifolia* aerial parts from the territory of Bosnia and Herzegovina differ from the results published so far. Antibacterial assay indicated that the mentioned essential oil showed antibacterial activity. It may help to identify and develop new effective antimicrobial agent. Further study is needed to purify and characterize the active compounds.

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KEY WORDS: *Inula verbascifolia*, aerial parts, essential oil, antimicrobial activity.

ORALNA PREZENTACIJA

BILJNI PREPARATI U TERAPIJI GOJAZNOSTI – BENEFIT I RIZIK

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UVOD I CILJ

Prevalenca gojaznosti dostiže epidemijske razmjere širom svijeta, pa se gojaznost svrstava među vodeće bolesti savremene civilizacije. Gojaznost dovodi do ozbiljnih zdravstvenih komplikacija, značajnog povećanja morbiditeta i mortaliteta i predstavlja globalni javnozdravstveni problem. S obzirom na mali broj konvencionalnih ljekova koji utiču na procese regulacije tjelesne težine i na njihove ozbiljne neželjene efekte, biljni preparati predstavljaju alternativu u terapiji gojaznosti. Cilj ovog preglednog rada obuhvatao je analizu aktivnih principa biljaka čija je efikasnost u terapiji gojaznosti potvrđena studijama, sa posebnim fokusom na mehanizme djelovanja i neželjena dejstva.

METODE

Analiza je izvršena sistematskim pregledom objavljenih kliničkih studija na animalnim i humanim modelima vezanih za efikasnost i bezbijednost ljekovitih biljaka u terapiji gojaznosti. Pregled literature je obavljen pretraživanjem elektronskih baza podataka - PubMed, Embase, Natural Medicines, Cochrane Library i Google Scholar, korišćenjem deskriptora "gojaznost", "ljekovite biljke" "efikasnost" i " bezbijednost "na engleskom jeziku, bez ograničenja vremenskog perioda. Analizirani su aktivni principi biljaka zastupljeni u proizvodima koji se prometuju u Crnoj Gori.

REZULTATI

Najčešće upotrebljivani preparati za redukciju tjelesne težine izrađeni su na bazi katehina lista zelenog čaja, koji povećavaju postprandijalnu termogenezu i oksidaciju lipida, inhibišu pankreasnu lipazu, smanjuju adipogenezu i utiču na supresiju apetita [1]. Antrahinonski heterozidi ispoljavaju laksativni efekat i predstavljaju komponente brojnih preparata za mršavljenje. Biljni diuretici su takođe prisutni u čajnim mješavinama i fitopreparatima. U novije vrijeme sve više se koriste preparati na bazi sinefrina čija je aktivnost stimulacija lipolize [2] i glukomanana koji dovodi do osjećaja sitosti [3]. Primjena biljnih preparata može biti kontraindikovana kod određenih fizioloških stanja i/ili oboljenja, uz pojavu interakcija sa konvencionalnim ljekovima, a njihova kontinuirana i dugotrajna upotreba kao i primjena većih doza od propisanih, može dovesti do ozbiljnih neželjenih efekata.

ZAKLJUČCI

Iako pokazuju zadovoljavajuće efekte u terapiji gojaznosti, samomedikacija prirodnim - biljnim preparatima nije preporučljiva. Realna činjenica je da „bezbijedno" i „prirodno" nisu sinonimi.

LITERATURA

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KLJUČNE RIJEČI: gojaznost, ljekovite biljke, efikasnost, bezbijednost

HERBAL REMEDIES IN THETREATMENT OF OBESITY – BENEFIT AND RISK

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INTRODUCTION AND OBJECTIVE:
The prevalence of obesity is reaching epidemic proportions worldwide making it one of the leading diseases of modern civilization. Obesity leads to serious health complications, significant increases morbidity and mortality and it is a global public health problem. Considering the small number of conventional drugs that affect the processes of weight regulation and their serious side effects, herbal remedies are an alternative in the treatment of obesity. The aim of this review paper was to analyze the active principles of plants whose efficacy in obesity therapy has been validated by studies, with a particular focus on mechanisms of action and side effects.

METHODS: The analysis was performed by a systematic review of published clinical studies on animal and human models related to the efficacy and safety of medicinal plants in obesity therapy. The literature review was performed by searching the electronic databases - PubMed, Embase, Natural Medicines, Cochrane Library and Google Scholar, using the descriptors "obesity", "medicinal herbs", "efficiency" and "safety" in English, without time limit. The active compounds of plants represented in products marketed in Montenegro were analyzed.

RESULTS: Commonly used weight loss preparations are catechin-based green tea leaves, which increase postprandial thermogenesis and lipid oxidation while inhibit pancreatic lipase, reduce adipogenesis, and act on appetite suppression [1]. Anthraquinone heteroids manifest a laxative effect and they are components of numerous weight loss preparations. Herbal diuretics are also present in tea mixtures and phytopreparations. More recently, synephrine-based preparations whose activity is stimulation of lipolysis [2] and glucomannan leading to satiety are increasingly used [3]. The use of herbal remedies may be contraindicated in certain physiological conditions and / or diseases, with the occurrence of interactions with conventional medicines and their continued and long-term use as well as administration of higher doses than prescribed can lead to serious side effects.

CONCLUSIONS:
Although they show satisfactory effects in obesity therapy, self-medication with herbal (natural) remedies is not recommended. The real fact is that "safe" and "natural" are not synonymous.

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KEY WORDS: obesity, medicinal herbs, efficiency andsafety

POSTER

ODREĐIVANJE ANTIOKSIDATIVNOG KAPACITETA PLODA RUŠVICE (*Amelanchier ovalis* MEDIK.)

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UVOD I CILJ

Polifenoli, a posebno flavonoidi, predstavljaju najviše ispitivanu grupu sekundarnih biljnih metabolita. Zahvaljujući specifičnoj hemijskoj strukturi, polifenoli djeluju kao snažni antioksidansi, što je osnova njihovog povoljnog i preventivnog djelovanja kod niza hroničnih bolesti uzrokovanih oksidacijskim stresom, kao što su kardiovaskularne i plućne bolesti, dijabetes tipa 2, tumori i sl. [1,2]. Cilj rada bio je ispitati sadržaj ukupnih fenolnih komponenata u plodu rušvice (*Amelanchier ovalis* Medik.) i odrediti njihovu antioksidativnu aktivnost.

METODE

Za određivanje fenolnih spojeva korištene su spektrofotometrijske metode: Folin-Ciocalteau, Vanilin-HCl i metoda sa aluminij(III)hloridom, a antioksidativna aktivnost ispitana je pomoću sljedećih *in vitro* testova: DPPH, FRAP, TEAC i određivanjem ukupnog antioksidativnog kapaciteta. Ispitana su dva uzorka: vodeni ekstrakt svježih plodova rušvice (uzorak 1) i vodeni ekstrakt pripremljen od plodova prethodno čuvanih u zamrzivaču (uzorak 2).

REZULTATI

Tabela 1. *Rezultati ispitivanja*

	Uzorak 1	Uzorak 2
Sadržaj ukupnih fenola (mg/L TA)	414,79	166,78
Neflavonoidni	50,47	27,7
Flavonoidni	364,32	139,08
Sadržaj ukupnih antocijanidina (mg/L katehina)	211,49	163,63
Sadržaj ukupnih flavonoida (mg/L katehina)	46,74	37,56
Procenat inhibicije DPPH	30,77	24,28
EC_{50}	2,24	2,81
FRAP vrijednosti (mM Fe^{2+}/L)	19,52	19,14
Ukupni antioksidativni kapacitet (mg/L askorbinske kiseline)	100,03	79,64
Antioksidativna aktivnost kao TEAC (TE, mmol/L)	9,20	7,38

ZAKLJUČCI

U radu je prikazan širok spektar metoda za određivanje fenolnih spojeva i njihove antioksidativne aktivnosti. Ukupni fenoli (flavonoidni i neflavonoidni) određeni su Folin-Ciocalteau metodom, antocijanidini Vanilin-HCl metodom a sadržaj ukupnih flavonoida kolorimetrijskom metodom sa aluminij(III)hloridom. Antioksidativni kapacitet određen je primjenom sljedećih *in vitro* testova: DPPH, FRAP, TEAC i određivanjem ukupnog antioksidativnog potencijala. Sadržaj fenolnih spojeva i njihova antioksidativna aktivnost bili su nešto veći u vodenom ekstraktu pripremljenom od svježih plodova rušvice (Tabela 1).

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KLJUČNE RIJEČI: fitohemikalije, polifenoli, antioksidativni kapacitet

DETERMINATION OF ANTIOXIDATIVE CAPACITY OF JUNEBERRIES (*Amelanchier ovalis* MEDIK.)

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INTRODUCTION AND OBJECTIVE

Polyphenols, especially flavonoids, are the most examinated group of secundary plant metabolites. Thanks to their chemical structure, they are strong antioxidants, which is the base of their beneficial and preventive effects in many chronical diseases caused by oxidative stress, like cardiovascular and respiratory diseases, diabetes mellitus type 2, tumors etc. [1,2]. The main objectives of this paper were to determine the total amount of polyphenolic compounds in juneberries (*Amelanchier ovalis* Medik.).

METHODS

The spectrofotometric methods used for the determination of phenolic compounds are: Folin-Ciocalteaeu, Vanilin-HCL and method with aluminium(III)chloride and antioxidative activity was determined by following *in vitro* tests: DPPH, FRAP, TEAC and determination of the total antioxidant potential.

Two samples were examinated: water extract of fresh juneberries (Sample 1.) and water extract prapared from previously freezed berries (Sample 2.).

RESULTS

Table 1. *Examination results*

	Sample 1	Sample 2
The amount of total phenols (mg/L TA)	414,79	166,78
flavonoid	50,47	27,7
non-flavonoid	364,32	139,08
The amount of total anthocianidines (mg/L katehina)	211,49	163,63
The amount of total flafonoids (mg/L katehina)	46,74	37,56
% DPPH inhibition	30,77	24,28
EC_{50}	2,24	2,81
FRAP values (mM Fe^{2+}/L)	19,52	19,14
Total antioxidative capacity (mg/L ascorbic acid)	100,03	79,64
Antioxidative activity like TEAC (TE, mmol/L)	9,20	7,38

CONCLUSIONS

This work shows a wide spectre of methods for determination of phenolic compounds and their antioxidative activites. Total phenols (flavonoids and non-flavonoids) were determined by Folin-Ciocalteaeu method, anthocianidines Vanillin-HCl method and the content of the total flavonoids with colorimetric method with aluminium(III)chloride. The antioxidant capacity is determined by applying the following *in vitro* tests: DPPH, FRAP, TEAC and determination of the total antioxidative potential. The content of the phenolic compounds and their antioxidant activity were somewhat bigger in water extract prepared from fresh fruits of juneberry (Table 1.)

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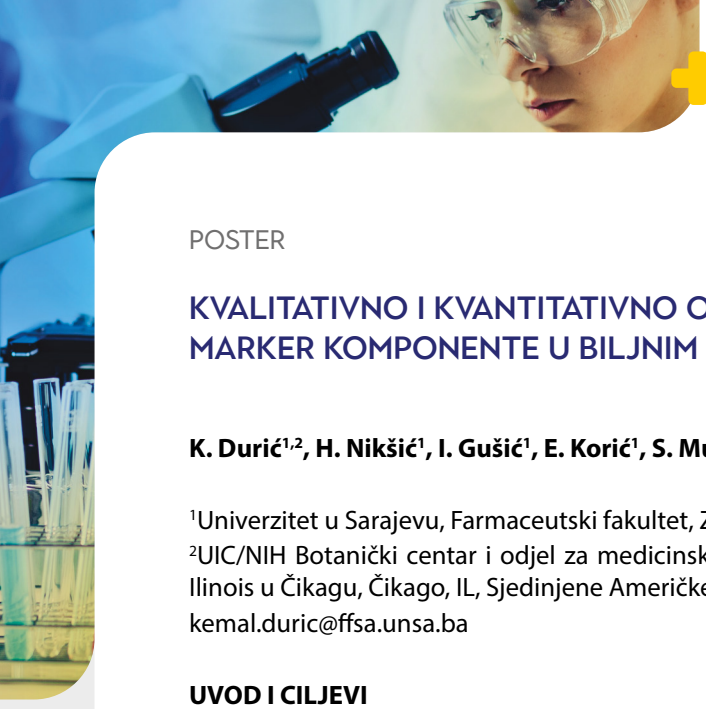
KEY WORDS: phytochemicals, polyphenols, antioxidative capacity



POSTER

KVALITATIVNO I KVANTITATIVNO ODREĐIVANJE LIGUSTILIDA KAO AKTIVNE MARKER KOMPONENTE U BILJNIM VRSTAMA PORODICE APIACEAE

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UVOD I CILJEVI

Veliki broj farmakoloških aktivnosti se povezuje sa ligustilidom, supstancom prisutnom u korijenu *A. sinesis*, koji se najčešće koristi u tretmanu poremećaja menstrualnog ciklusa i premenstrualnog sindroma. Nedavno provedena farmakološka istraživanja potvrđuju da biljne vrste-droge koje sadrže ligustilid imaju antiinflamatorno djelovanje i pozitivan učinak na kognitivne sposobnosti, ublažavaju oštećenja na nivou moždanih struktura, inhibiraju tumor nekrozni faktor određenih ćelijskih linija, imaju protektivno djelovaje na nivou bubrega kao i neuroprotektivno djelovanje. U ovom radu, urađena je kvantifikcija ligustilida pomoću qHNMR metode u hermetički zatvorenim NMR epruvetama.

METODE

Ispitane su četiri ligustilidom bogate biljne vrste: *A. sinensis*, *Ligusticum porteri*, *L. striatum*, and *L. sinense*. Većina ftalida, uključujući i ligustilid, su relativno nepolarne molekule, i dio su eteričnih ulja koja se nalaze u navedenim biljkama. Tehnike ekstrakcije koje se mogu koristiti uključuju različita otapala, ekstrakciju vodenom parom i ekstrakciju superkritičnim gasovima. U ovom radu ekstrakcija eteričnih ulja iz korijena navedenih biljnih vrsta provedena je modifikovanom metodom superkritičnim gasom CO_2. Procenat zastupljenosti ligustilida u eteričnim uljuma izračunat je metodom qHNMR.

REZULTATI

Prinos eteričnog ulja na 100 grama droge je sljedeći: radix Angelicae sinensis 1.5 g; radix Ligusticum striatum 1.6 g; radix Ligusticum sinense 0.35 g; radix Ligusticum porteri 7.3 g. Obzirom na hemijsku nestabilnost molekule ligustilida, isti je kvantifikovan u hermetički zatvorenim NMR epruvetama. qHNMR analiza procenta ligustilida u četiri ispitivana ulja je dala sljedeće rezultate: eterično ulje L. porteri 3.74%; eterično ulje L. sinense 1.16 %; eterično ulje L. striatum 6.61% i eterično ulje A. sinensis 14.56%.

ZAKLJUČCI

Eterična ulja su dobivena ekstrakcijom superkritičnim gasom CO_2. Modifikovana procedura ekstrakcije superkritičnim CO_2 se pokazala boljom jer je dala veći procentualni prinos ulja i ligustilida u ulju. Najveći procenat ulja je dobiven iz korijena *L. Porteri*, ali je najveći procenat ligustilida određen u eteričnom ulju *Angelica sinensis*.

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KLJUČNE RIJEČI: Ligustilid, qHNMR, porodica Apiaceae

QUALITATIVE AND QUANTITATIVE DETERMINATION OF LIGUSTILIDE AS A BIOACTIVE MARKER IN APIACEAOUS BOTANICALS

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INTRODUCTION AND OBJECTIVE

Variety of bioactivities has been associated with ligustilide present in root of *A. sinensis*, predominantly used for the treatment of irregular menstrual cycles and premenstrual syndrome. Recent pharmacological studies showed that medicinal plants containing ligustilide, have anti-inflammatory effects and improvement in cognitive functions, alleviate brain damage, inhibit tumor necrosis factor of some cell lines, nephron-protective effects and neuroprotective activity. In this work, quantification of ligustilide using quantitative 1H NMR in sealed tubes was performed.

METOHODS

Four ligustilide-rich species were investigated: *A. sinensis*, *Ligusticum porteri*, *L. striatum*, and *L. sinense*. Majority of phthalides, ligustilide included, being relatively non-polar, are parts of essential oils in their plant of origin. Extraction techniques that could be used include different organic solvent extraction, steam distillation and extraction with supercritical gas. In this work extraction of essential oil from root of four investigated species, with modified supercritical CO2 method was performed. Average of of ligustilide in essential oils was quantified using qHNMR.

RESULTS

The yield of essential oil per 100 g of dry plant material was as follows: radix Angelicae sinensis 1.5 g; radix Ligusticum striatum 1.6 g; radix Ligusticum sinense 0.35 g; radix Ligusticum porteri 7.3 g. Given the instability of the ligustilide molecule, the same was quantified in NMR tubes sealed with flame. qHNMR analisys showed following percentage of ligustilide in four essential oil: L. porteri essentia oil 3.74 (%); L. sinense essential oil 1.16 (%); L. striatum essential oil 6.61 (%) and A. Sinensis essential oil 14.56 (%).

CONCLUSIONS

Essential oils were gently obtained by supercritical CO_2 fluid extraction. Modified procedure for SFE extraction from different plant materials provides better yield of ligustilide. The highest percentage of oil was obtained from the root of L. porteri but the highest percentage of ligustilide showed essential oil from Angelica sinensis.

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KEY WORDS: Ligustilide, qHNMR, Apiaceae family

POSTER

TRADICIONALNA ETNOMEDICINA KAO IZVOR NOVIH KOZMECEUTIKA

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UVOD I CILJ

Strukturne promjene kože nastaju kao prirodna posljedica starenja, te pod utjecajem unutarnjih i vanjskih čimbenika. Manifestiraju se u obliku upalnih procesa, promjena pigmentacije, elastičnosti ili hidratacije kože koji su zajedno poznati kao starenje kože. Djelomično se takvi procesi mogu spriječiti upotrebom različitih kozmetičkih proizvoda, a posebnu popularnost uživaju proizvodi s biljnim aktivnim sastojcima. U ovom radu istraženo je nekoliko biljaka koje se koriste za liječenje kožnih bolesti u hrvatskoj etnomedicini kako bi se procijenio njihov fitokozmetički potencijal.

METODE

U radu je ispitan anti-age i antioksidacijski potencijal bljnih vrsta *Achilea millefolium*, *Brasica oleracea*, *Centaurea jacea*, *Cychorium intybus*, *Knautia arvensis*, *Lotus corniculatus*, *Medicago lupulina*, *Malva neglecta Medicago sativa*, *Plantago lanceolata*, *Plantago major*, *Olea europaea*, *Trifolium pretense* i *Arthrospira* sp. Ispitivanje je provedeno u mikrotitarskim pločicama s 96 jažica. Ekstrakti su pripremljeni korištenjem mješavina vode s različitim udjelima etanola. Inhibicija tirozinaze, elastaze i kolagenaze ispitivana je korištenjem odgovarajućih enzima. Antioksidativno djelovanje ispitano je β-karoten-linoleatnom te u ORAC testu. Aktivnosti su izračunate korištenjem regresijske analize i izražene kao IC_{50} vrijednosti.

REZULTATI

Ispitane biljke bile su slabi do umjereni inhibitori elastaze s aktivnošću koja je iznosila 1-6 mg/mL. Aktivnost inhibicije tirozinaze, s druge strane, bila je u rasponu od 750-2500 µg/mL. IC_{50} vrijednost inhibicije kolagenaze bila je između 45-600 µg/mL. Najaktivnije biljke u navedenim testovima bile su *Olea europaea*, *Knautia arvensis* odnosno *Lotus coriculatus*. Ispitivane biljke pokazale su dobar antioksidativni potencijal što je dodatno pridonijelo njihovoj potencijalnoj primjeni u proizvodina za kožu.

ZAKLJUČCI

Jedanaest biljaka koje se u hrvatskoj etnomedicini koriste za tretman kožnih oboljenja ispitano je pomoću nekoliko enzimskih i antioksidativnih *in vitro* metoda. Značajan antioksidativni i anti-age potencijal odabranih ljekovitih biljaka čini ih prikladnim sastojcima prirodne kozmetike i kozmeceutika.

KLJUČNE RIJEČI: kozmeceutici, tradicionalna medicina, antioksidansi, anti-age

TRADITIONAL MEDICINE AS SOURCE OF NEW COSMECEUTICALS

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INTRODUCTION AND OBJECTIVE

Structural changes of skin occur as a natural consequence of ageing, as well as under the influence of internal and external factors. They manifest in the form of inflammatory processes, changes in pigmentation, elasticity or skin hydration, together known as skin aging. Partially, such processes can be prevented by using various cosmetic products, with particular popularity being enjoyed by products with herbal active ingredients. In this work several plants used for treatment of skin diseases in Croatian ethnomedicine was investigated in order to estimate their phytocosmeceutical potential.

METHODS

In this work anti-ageing and antioxidant potential of *Achilea millefolium*, *Brasica oleracea*, *Centaurea jacea*, *Cychorium intybus*, *Knautia arvensis*, *Lotus corniculatus*, *Medicago lupulina*, *Malva neglecta Medicago sativa*, *Plantago lanceolata*, *Plantago major*, *Olea europaea*, *Trifolium pretense* and *Arthrospira* sp was investigated by screening in 96-well microtiter plates. The extracts were prepared using the mixtures of water with varying proportions of ethanol. Anti-tyrosinase, anti-elastase and anti collagenase properties were investigated using the appropriate enzymes. Antioxidant activity was investigated in β-carotene-linoleic acid assay and in ORAC test. The activities were calculated using regression analysis and expressed as IC_{50} values.

RESULTS

The investigated plants were weak to moderate elastase inhibitors with the observed activity in approximate range 1-6 mg/mL. Anti-tyrosinase activity, on the other hand was in 750-2500 µg/mL range. The activity in anti-collagenase assay spanned between 45-600 µg/mL. The most active plants in the performed assays were *O. europaea*, *K. arvensis* and *L. coriculatus*, respectively. The investigated plants showed good antioxidant abilities which further contributed to their cosmeceutical potential.

CONCLUSIONS

Eleven plants used for skin-related diseases in Croatian ethnomedicine were screened in various enzymatic and antioxidant *in vitro* assays. The observed good antioxidant and anti-aging potential of selected medicinal plants renders them suitable for inclusion in natural cosmetics and cosmeceutical products.

KEY WORDS *cosmeceutical, traditional medicine, antioxidant, anti-age*

POSTER

ANTIFUNGALNA I ANTIOKSIDATIVNA AKTIVNOST ETERIČNOG ULJA *ORIGANUM COMPACTUM* BENTH.

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UVOD I CILJEVI

Origanum compactum Benth. *(O. compactum)*, lokalno poznat u Maroku kao za'tar, endemska je marokanska ljekovita biljka. Brojna su istraživanja pokazala da organski ekstrakti *O. compactum*, eterično ulje i njegove glavne komponente posjeduju širok spektar farmakoloških i terapijskih aktivnosti poput antibakterijskih, antifungalnih, antioksidativnih i antikancerogenih aktivnosti [1, 2]. Cilj ovog rada bio je ispitivanje antifungalnog i antioksidativnog djelovanja esencijalnog ulja *O. Compactum* Benth.

METODE

U ovom istraživanju korišteno je eterično ulje *O. compactum* Benth. od firme Pranarom International (Ghislenghien, Belgija). Antifungalna aktivnost *O. compactum* izvedena je na kliničkim sojevima *Candida albicans (C. albicans)* primjenom metode agar difuzije prema CLSI smjernicama uz neke modifikacije [3]. Klinički sojevi su izolirani iz vaginalnih i cervikalnih briseva, od pacijentica na Univerzitetskom kliničkom centru Tuzla (BIH). Antioksidantna aktivnost testirana je DPPH metodom. Askorbinska kiselina je korištena kao pozitivna kontrola, a metanol kao negativna kontrola.

REZULTATI

Eterično ulje *O. compactum* pokazalo je snažnu antifungalnu aktivnost, a zone inhibicije (IZ) su bile od 31.0 mm do 45.0 mm. Antifungalna aktivnost testirana je na dvadeset kliničkih sojeva *C. albicans*. DPPH test je najčešće korištena *in vitro* metoda za određivanje antioksidativne aktivnosti biljnih ekstrakata i eteričnih ulja. IC_{50} za eterično ulje *O. compactum* iznosio je 0.390 mg/mL, a za askorbinsku kiselinu 0.084 mg/mL.

ZAKLJUČAK

Na osnovu dobijenih rezultata možemo zaključiti da eterično ulje *O. compactum* ima snažno antifungalno i antioksidativno djelovanje. Eterično ulje *O. compactum* moglo bi biti idealna zamjena za konvencionalne antimikrobne proizvode i moglo bi biti opcija u liječenju ginekoloških gljivičnih infekcija. Naši rezultati za antioksidativno djelovanje usklađeni su s drugim istraživanjima koja su izvijestila da eterično ulje *O. compactum* posjeduje snažno antioksidativno djelovanje te se može koristiti kao prirodni konzervans u prehrambenoj i/ili farmaceutskoj industriji.

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KLJUČNE RIJEČI: *Origanum compactum*, eterično ulje, antioksidativno djelovanje, antifungalno djelovanje, *Candida albicans*

ANTIFUNGAL AND ANTIOXIDANT ACTIVITY OF *ORIGANUM COMPACTUM* BENTH. ESSENTIAL OIL

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INTRODUCTION AND OBJECTIVE

Origanum compactum Benth. (*O. compactum*), locally known as za'tar in Morocco, is an endemic Moroccan medicinal herb. Numerous studies showed that the *O. compactum* organic extracts, essential oil and its main components possess a broader spectrum of pharmacological and therapeutic activities such as antibacterial, antifungal, antioxidant and anticancer activity [1, 2]. The aim of this work was to investigate antifungal and antioxidant activity of *O. compactum* Benth. essential oil.

METHODS

In this study was used *O. compactum* Benth. essential oil by Pranarom International (Ghislenghien, Belgique). Antifungal activity of *O. compactum* was performed on clinical strains of *Candida albicans (C. albicans)* using agar diffusion method according to CLSI guidelines with some modifications [3]. Clinical strains were collected from vaginal and cervical swabs, from patients at the University Clinical Center Tuzla (BIH). Antioxidant activity was tested using DPPH method. Ascorbic acid was used as positive control, and methanol as negative control.

RESULTS

O. compactum essential oil showed a strong antifungal activity, and the inhibition zones (IZ) were from 31.0 mm to 45.0 mm. Antifungal activity was tested on twenty clinical strains of *C. albicans.* DPPH test is most commonly *in vitro* method for antioxidant activities determination of plant extracts and essential oils. IC_{50} for *O. compactum* essential oil was 0.390 mg/mL, and for ascorbic acid was 0.084 mg/mL.

CONCLUSION

According to the obtained results we can conclude that *O. compactum* essential oil has a strong antifungal and antioxidant activity. *O. compactum* essential oil could be an ideal replacement for conventional antimicrobial products and could be an option in treatment of gynecological fungal infections. Our results of antioxidant activity are in accordance with other studies who reported that essential oil of *O. compactum* possesses strong antioxidant activity, and therefore can be used as natural preservative in food and/or pharmaceutical industry.

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KEY WORDS: *Origanum compactum*, essential oil, antioxidant activity, antifungal activity, *Candida albicans*

POSTER

KVALITATIVNA I KVANTITATIVNA ANALIZA TRITERPENA U VRSTAMA PORODICE LAMIACEAE

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UVOD I CILJEVI

Triterpeni se konstantno povezuju sa dokazanim djelovanjem koji imaju ekstrakti dobijeni iz biljnog materijala koji sadrže ove vrlo važne metabolite sekundarnog biljnog metabolizma. Veliki broj vrsta iz porodice Lamiaceae se koristi radi prisustva eteričnog ulja, ali se malo zna o prisustvu triterpesnkig supstanci u ovoj porodici. U ovom radu provedena je kvalitativna i kvantitativna analiza ovih važnih supstanci i to u nadzemnim dijelovima *Mentha piperita* L., *Thymus pulegioides* L., *Rosmarinus officinalis* L., *Origanum vulgare* L., *Salvia officinalis* L., *Satureja montana* L., *Lavandula officinalis* L. and *Melissa officinalis* L., vrstama porodice Lamiaceae.

METODE

Soxhlet aparatura je korištena sa ciljem pripreme heksanskog, hloroformskog i metanolnog ekstrakta. Metode hromatografije na tankom sloju i tečna hromatografija pod visokim pritiskom su korištene za kvalitativnu i kvatitativnu analizu triterpena u različitim ekstraktima. Korišteni su različiti uslovi za pomenute separacione metode sa ciljem utvrđivanja najboljih uslova za razdvajanje betulina, betulinske kiseline, ursolne kiseline i oleanolne kiseline.

REZULTATI

Nakon provedene sukcesivne ekstrakcije različitim otapalima, dokazano je da hloroformska i heksanska frakcija sadrže najveću količinu triterpenskih supstanci. Rezultati hromatografije na tankom sloju i tečne hromatografije pod visokim pritiskom potvrđuju prisustvo betulina, betulinske kisline, urslone kiseline, oleanolne kisline i lupeola. Betulin (3,2 mg/g) i betulinska kiselina (37,1 mg/g) su bili najzastupljenije triterpenske supstance u heksanskom ekstraktu *Rosmarinus officinalis L*. Ursolna kiselina (0,14 mg/ml) je bila najzastupljenija supstanca u ekstraktu *Thymus pulegioides L*.

ZAKLJUČCI

Rezultati dobijeni ovim istraživanjem potvrđuju prisustvo triterpena u ispitivanom biljnom materijalu. Navedeno sugerira mogućnost pleiotropnog učinka ispitivanih biljnih vrsta i njihovu mogućnost upotrebe u farmaciji i medicine sa stanovišta prisustva triterpenskih supstanci.

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KLJUČNE RJEČI: Lamiaceae, triterpeni, ekstrakcija

QUALITATIVE AND QUANTITATIVE ANALYSIS OF TRITERPENES IN PLANT SPEICIES FROM LAMIACEAE FAMILY

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INTRODUCTION AND OBJECTIVE

Triterpenes are persistently associated with observed bioactivities of extracts obtained from plant material that contains these very important natural products. Many species belonging to Lamiaceae family have been used for the presence of essential oil and very little is known about the presence of the triterpene substances in this family. Qualitative and quantitative analyses of this very important substances, in the aerial parts of *Mentha piperita* L., *Thymus pulegioides* L., *Rosmarinus officinalis* L., *Origanum vulgare* L., *Salvia officinalis* L., *Satureja montana* L., *Lavandula officinalis* L. and *Melissa officinalis* L., all belonging to Lamiaceae family, were investigated in this study.

METOHODS

Soxhlet apparatus was used in order to prepare hexane, chloroform and methanol extracts. Method of thin layer chromatography and high pressure liquid chromatography were used for qualitative and quantitative analysis of triterpenes in different extracts. Different conditions for this separation method were used in order to find out the best conditions for separation of betulin, betulinic acid, ursolic acid and oleanolic acid.

RESULTS

After successive extraction with different solvents has been performed, it was found that hexane and chloroform fractions contained the most considerable amount of triterpene substances. The thin layer chromatography and the high-pressure liquid chromatography results confirmed the presence of betulin, betulinic acid, ursolic acid, oleanolic acid and lupeol. Betulin (3.2 mg/g) and betulinic acid (37.1 mg/g) were the most abundant triterpene components in the hexane extracts of Rosmarinus officinalis L. Ursolic acid (0.14 mg/ml) was the most abundant triterpene compound in the hexane extract of Thymus pulegioides L.

CONCLUSIONS

The results obtained by this investigation confirm the presence of triterpenes in investigated plant materials. This suggest the new potential pleiotropic properties of the investigated plant species and their possible use in official pharmacy and medicine from the point of view of the presence of triterpenes.

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KEY WORDS: Lamiaceae family, triterpenes, extraction

POSTER

KVALITATIVNA I KVANTITATIVNA ANALIZA POLIFENOLA VRSTE *MICROMERIA KOSANINII* ŠILIĆ (LAMIACEAE)

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UVOD I CILJEVI

Rod Micromeria Benth. (bresina) uključuje mnoge endemične i subendemične vrste koje su zbog ograničene rasprostranjenosti i nepristupačnih nalazišta slabo zastupljene u tradicionalnoj medicini, stoga ne čudi da danas zaokupljaju posebnu pozornost znanstvenika kao slabo istraženi potencijalni izvori ljekovitih tvari. *Micromeria kosaninii* Šilić višegodišnja je biljka iz porodice Lamiaceae koja raste u pukotinama stijena u planinskim područjima Makedonije, a 2013. godine pronađena je i u Nacionalnom parku Prespa u Albaniji [1]. Provedena je fitokemijska analiza polifenolnih spojeva iz nadzemnih dijelova makedonske endemične vrste *Micromeria kosaninii* (Lamiaceae).

METODE

Kvalitativna analiza polifenolnih spojeva u metanolnom ekstraktu vrste M. kosaninii provedena je kemijskim reakcijama stvaranja obojenih produkata i taloga te primjenom tankoslojne kromatografije (TLC) [2, 3]. Sadržaj polifenolnih tvari određen je različitim spektrofotometrijskim metodama: fenolne kiseline (FK; A_{505nm} i A_{525nm}), flavonoidi (F; A_{425nm}) te ukupni polifenoli i trjeslovine (UP i T; A_{720nm}) [4].

REZULTATI

Prisutnost polifenola u metanolnom ekstraktu vrste *M. kosaninii* potvrđena je kemijskim reakcijama stvaranja obojenih produkata i taloga. TLC analizom utvrđena je prisutnost flavonoida i fenolnih kiselina: naringina, kvercitrina, izokvercitrina, klorogenske, izoklorogenske, kavene i ružmarinske kiseline. Kvantitativnom spektrofotometrijskom analizom polifenola utvrđeno je sljedeće: sadržaj FK (izražen kao ružmarinska kiselina) iznosio je 4,30±0,21% ($A_{505\ nm}$), dok je sadržaj FK izražen na klorogensku kiselinu bio 7,97±0,37% (A_{525nm}); udio F iznosio je 0,07±0,01%; sadržaj UP bio je 8,62±0,13%, a udio T 2,76±0,15%.

ZAKLJUČCI

Provedena fitokemijska karakterizacija predstavlja doprinos dosadašnjem istraživanju roda Micromeria i makedonskih endema te upotpunjuje znanstvene spoznaje o biološkoj aktivnosti i fitoterapijskom potencijalu vrste *Micromeria kosaninii*.

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KLJUČNE RIJEČI: *Micromeria kosaninii*, polifenoli, tankoslojna kromatografija, UV-Vis spektrofotometrija

QUALITATIVE AND QUANTITATIVE ANALYSIS OF POLYPHENOLS OF *MICROMERIA KOSANINII* ŠILIĆ (LAMIACEAE)

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INTRODUCTION AND OBJECTIVE

The genus Micromeria Benth includes many endemic and sub-endemic species that are poorly represented in traditional medicine due to their limited distribution and inaccessible sites. So it is not surprising that today it attract the particular attention of scientists as poorly explored potential source of medicinal substances. *Micromeria kosaninii* Šilić is a perennial plant from the Lamiaceae family which grows in rock crevices in the mountain regions of Macedonia, and in 2013 was also found in the National Park Prespa in Albania [1]. In this study, phytochemical analysis of polyphenolic compounds from aerial parts of the Macedonian endemic species *M. kosaninii* (Lamiaceae) was performed.

METHODS

Qualitative analysis of polyphenolic compounds in methanolic extract of *M. kosaninii* was performed by chemical reactions and by thin layer chromatography (TLC) [2, 3]. The content of polyphenolic substances was determined by various spectrophotometric methods: phenolic acids (PA; A_{505nm} and A_{525nm}), flavonoids (F; A_{425nm}), and total polyphenols and tannins (TP and T; A_{720nm}) [4].

RESULTS

The presence of polyphenols in the methanolic extract of *M. kosaninii* was confirmed by the chemical reactions of the formation of characteristic colored products and precipitates. TLC analysis determined the presence of flavonoids and phenolic acids: naringin, quercitrin and isoquercitrin, as well as chlorogenic, isochlorogenic, caffeic and rosmarinic acids. Quantitative spectrophotometric analysis of polyphenols revealed the following: the PA content (expressed as rosmarinic acids) was 4.30%±0.21% ($A_{505\ nm}$), while the PA content expressed as chlorogenic acid was 7.97±0.37; the content of F was 0.07±0.01%; the TP content was determined in concentration of 8.62±0.13%, while the content of T was 2.76±0.15%.

CONCLUSIONS

The performed phytochemical characterization represents a scientific contribution to the current research of the genus Micromeria and the Macedonian endemic plant species, and also completes the existing knowledge about biological activity and phytotherapeutic potential of the species *Micromeria kosaninii.*

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KEY WORDS: *Micromeria kosaninii,* polyphenols, thin-layer chromatography, UV-Vis spectrophotometry

POSTER

SEZONSKA VARIJABILNOST SADRŽAJA UKUPNIH POLIFENOLA I TRJESLOVINA VRSTE *LAURUS NOBILIS* L. (LAURACEAE) IZ HRVATSKE

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UVOD I CILJ

Lovor (*Laurus nobilis* L., Lauraceae) krupni je grm ili stablo visine do 15 m, često uzgajano u nasadima primorskog područja kao ukrasna i začinska biljka. Lovor ima umjerenu antibakterijsku aktivnost, ali vrlo je aktivan protiv gljivica. Djeluje također kao spazmolitik, analgetik i ekspektorans [1]. U svrhu praćenja sezonske varijabilnosti sadržaja bioaktivnih polifenolnih tvari tijekom 12 mjeseci, te posljedično praćenja fitoterapijskog potencijala lovora, provedena je kvantitativna analiza sadržaja ukupnih polifenola (UP) i trjeslovina (T) iz listova lovora s područja Hrvatskog primorja (populacija Lovran), sabranih u razdoblju od svibnja 2015. do travnja 2016. godine.

METODE

Kvantitativna analiza UP i T provedena je UV-Vis spektrofotometrijskom metodom s Folin-Ciocalteuovim fenolnim reagensom (A_{720nm}, prema izvornoj metodi; A_{748nm}, maksimum apsorpcije) [2].

REZULTATI

Sadržaj ukupnih polifenola bio je najveći za uzorak lista lovora iz rujna 2015. godine i iznosio je 9,08% (A_{720nm}), odnosno 9,12% (A_{748nm}), dok je najmanja vrijednost zabilježena za uzorak iz svibnja 2015., i iznosila je 5,67% (A_{720nm}) te 5,80% (A_{748nm}). Analogno rezultatima dobivenim za UP, također je najveća količina T u listovima lovora zabilježena u uzorcima iz rujna 2015., i iznosila je 4,91% (A_{720nm}) te 4,87% (A_{748nm}), dok je najmanja vrijednost sadržaja T određena za uzorak iz svibnja 2015: 2,31% (A_{720nm}); 2,37% (A_{748nm}). Među navedenim se rezultatima ističe visok sadržaj polifenolnih tvari u veljači 2016., za razliku od ostalih zimskih mjeseci u praćenom razdoblju: UP (8,53% $A_{720nm;}$ 8,68%, A_{748nm}) i T (3,89%, A_{720nm}; 3,94%, A_{748nm}). To bi se moglo objasniti iznadprosječnom temperaturom zraka za to doba godine te velikom količinom padalina, što je potvrđeno uvidom u vremenske uvjete u Lovranu za 2016. godinu (podaci Državnog hidrometeorološkog zavoda).

ZAKLJUČCI

Provedena studija doprinosi znanstvenom istraživanju lovora i upotpunjuje dosadašnje spoznaje o sadržaju njegovih polifenolnih sastavnica, posebice u pogledu njihove sezonske varijabilnosti, što može pomoći u procjeni fitoterapijskog potencijala vrste *Laurus nobilis* L.

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KLJUČNE RIJEČI: *Laurus nobilis*, polifenoli, trjeslovine, UV-Vis spektrofotometrija, varijabilnost polifenolnog sadržaja

SEASONAL VARIABILITY OF THE CONTENTS OF TOTAL POLYPHENOLS AND TANNINS OF *LAURUS NOBILIS* L. (LAURACEAE) FROM CROATIA

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INTRODUCTION AND OBJECTIVE

Bay laurel (*Laurus nobilis* L., Lauraceae) is a large shrub or tree up to 15 m high, often grown in coastal areas as an ornamental and spicy plant. Laurel has moderate antibacterial activity but is very active against fungi. It also acts as a spasmolytic, analgesic and expectorant [1]. In order to monitor the seasonal variability of the content of bioactive polyphenolic substances during the 12 months (from May 2015 to April 2016), and consequently to monitor the phytotherapeutic potential of laurel, a quantitative analysis of the content of total polyphenols (TP) and tannins (T) from laurel leaves from the Croatian coast (Lovran population) was performed.

METHODS

Quantitative analysis of TP and T was performed by UV-Vis spectrophotometric method with Folin-Ciocalteu phenolic reagent (A_{720nm}, according to the original method; A_{748nm}, maximum absorption) [2].

RESULTS

The content of TP in the sample of laurel leaf was the highest for the September 2015 (9.08%, A_{720nm} and 9.12%, A_{748nm}), while the lowest content was recorded for the May 2015 (5.67%, A_{720nm} and 5.80%, A_{748nm}). By analogy with the results obtained for TP, the highest amount of T in the laurel leaves was also recorded in the September 2015, amounting to 4.91% (A_{720nm}) and 4.87% (A_{748nm}), while the lowest content of T was determined for the sample from May 2015 (2.31%, A_{720nm} and 2.37%, A_{748nm}). Among these results, the high content of polyphenolic substances in February 2016 stands out, in contrast to the other winter months in the observed period: TP (8.53%, A_{720nm}; 8.68%, A_{748nm}) and T (3.89%, A_{748nm}; 3.94%, A_{748nm}). This could be explained by the above-average air temperature for that time of the year and the large amount of precipitation, which was confirmed by the weather forecast in Lovran for 2016 (data from the Croatian Meteorological and Hydrological Service).

CONCLUSIONS

This quantitative analysis represents a contribution to scientific study of polyphenols and tannins in the leaves of *Laurus nobilis* and completes the previous knowledge about laurel's phytotherapeutic potential, especially in relation to the content of bioactive phenolic substances.

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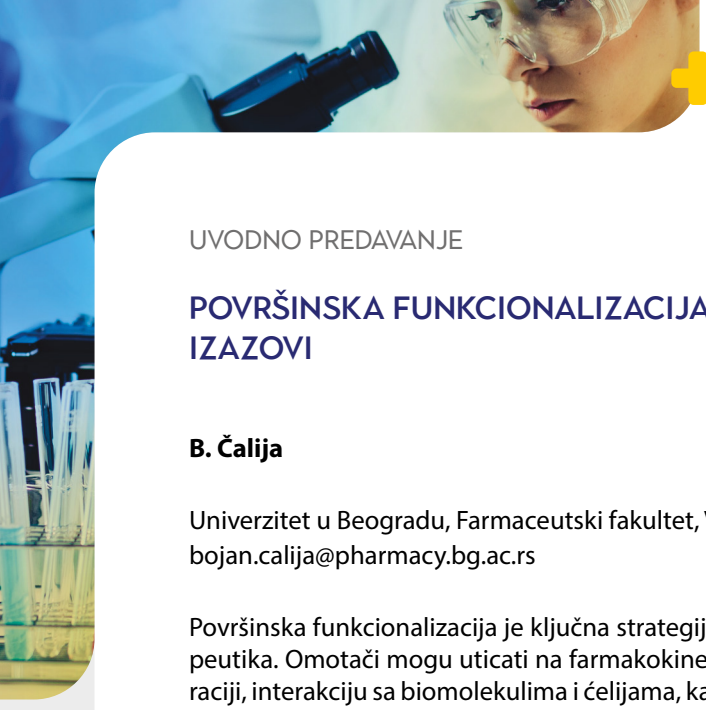
KEY WORDS: *Laurus nobilis*, polyphenols, tannins, UV-Vis spectrophotometry, seasonal polyphenol variations

FARMACEUTSKA TEHNOLOGIJA I KOZMETOLOGIJA



UVODNO PREDAVANJE

POVRŠINSKA FUNKCIONALIZACIJA NANOTERAPEUTIKA: MOGUĆNOSTI I IZAZOVI

B. Čalija

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Površinska funkcionalizacija je ključna strategija za poboljšanje terapijske efikasnosti i bezbednosti nanoterapeutika. Omotači mogu uticati na farmakokinetiku i biodistribuciju nanonosača, njihovu sklonost ka aglomeraciji, interakciju sa biomolekulima i ćelijama, kao i na metaboličke puteve inkapsuliranih aktivnih supstanci [1]. Funkcionalnost omotača zavisi od njegovog hemijskog sastava, ujednačenosti, načina vezivanja za površinu nanonosača (kovaletno ili nekovalentno), gustine, orjentacije i konformacije liganada, *in vitro* i *in vivo* stabilnosti i fizičko-hemijskih karakteristika površine za koju je vezan [1,2].

Za površinsku funkcionalizaciju nanonosača najčešće se koriste polietilenglikoli, proteini i peptidi (antitela), aptameri, poligliceroli, polioksazolini, vinil polimeri, ugljeni hidrati i surfaktanti (polisorbati i poloksameri) [2,3]. Njihovu primenu, pored primarne hemijske strukture, determinišu molekulska masa, dužina lanaca, prostorna orjentacija, hidrofilnost/hidrofobnost, sposobnost jonizacije, stabilnost i biokompatibilnost. Površinskom funkcionalizacijom hidrofilnim polimerima, poput polietilenglikola, moguće je produžiti poluvreme eliminacije nanonosača usled sternog ometanja opsonizacije, umanjiti njihovu sklonost ka aglomeraciji i poboljšati rastvorljivost [2]. Međutim, površinska funkcionalizacija polietilenglikolima može negativno uticati na ćelijsko preuzimanje i beg nanonosača iz endozoma, te posledično smanjiti intraćelijski nivo aktivne supstance u ciljnom tkivu. Nasuprot tome, hidrofobni omotači generalno ispoljavaju efikasnije kontrolisano oslobađanje i poboljšano ćelijsko preuzimanje [2]. Stoga je potrebno pažljivo izbalansirati svojstva omotača kako bi se postigla zadovoljavajuća terapijska efikasnost, stabilnost i bezbednost finalnog proizvoda.

U okviru ovog predavanja biće diskutovani različiti pristupi površinskoj funkcionalizaciji nanoterapeutika sa akcentom na aktuelna istraživanja u ovoj oblasti, primere registrovanih lekova i trenutne regulatorne okvire.

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KLJUČNE RIJEČI: nanoterapeutici, omotač, ciljano delovanje, opsonizacija, ćelijsko preuzimanje

SURFACE FUNCTIONALIZATION OF NANOTHERAPEUTICS: POSSIBILITIES AND CHALLENGES

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Surface functionalization is a major strategy to improve efficacy and safety of nanotherapeutics. Coatings may affect pharmacokinetics and biodistribution of drug nanocarriers, their tendency to agglomerate, interaction with biomolecules and cells, and metabolic pathways of the entrapped actives [1]. Functionality of the coating is governed by its chemical composition, uniformity, nature of surface bonding (covalent or non-covalent), density, orientation and conformation of ligands, coating stability *in vitro* and *in vivo* and physico-chemical characteristics of the surface to which it is attached [1,2].

Commonly used coating agents are polyethylene glycols, proteins and peptides (antibodies), aptamers, polyglycerols, poly(2-oxazoline)s, vinyl polimers, carbohydrates, and surfactants (polisorbates and poloxamers) [2,3]. In addition to primary chemical structure, their critical attributes are molar mass, chain length, conformation, hydrophilicity/hydrophobicity, ionization ability, stability and biocompatibility. Coating of nanocarriers with hydrophilic polymers, such as polyethylene glycols, may increase their half-life by preventing opsonization, reduce their tendency to agglomerate and improve their solubility [2]. However, surface functionalization with these polymers may have negative effect on cellular uptake and endosomal escape, with consequent decrease in intracellular drug level in target tissue. In contrast, hydrophobic coatings generally provide more effective controlled release and cellular uptake [2]. Therefore, coating properties have to be carefully balanced and tailored to achieve acceptable efficacy, stability and safety of the final drug product.

Various approaches of nanotherapeutics surface functionalization will be discussed with focus on state-of-the art research in this field, examples of approved medicines and current regulatory framework.

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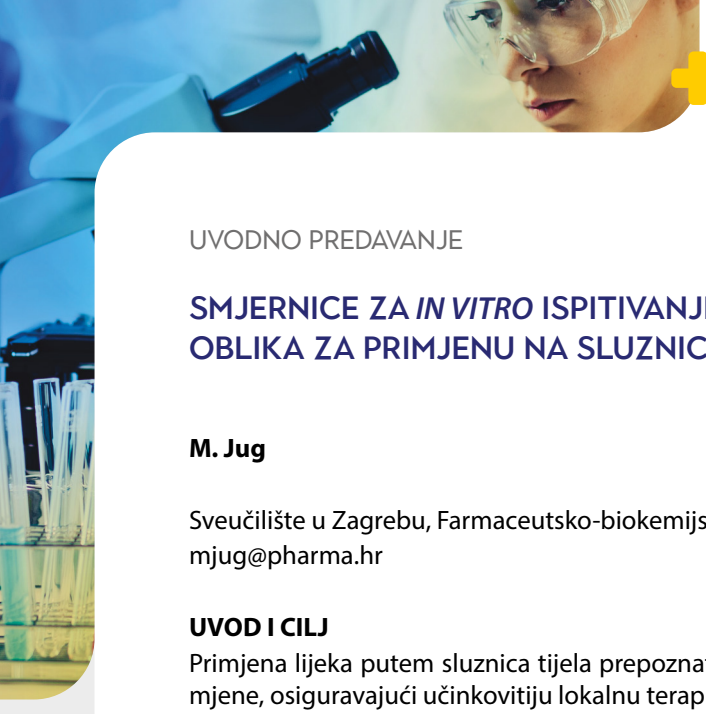
KEY WORDS: nanotherapeutics, coating, target-delivery, opsonization, cellular uptake



UVODNO PREDAVANJE

SMJERNICE ZA *IN VITRO* ISPITIVANJE OSLOBAĐANJA LIJEKA KOD SUVREMENIH OBLIKA ZA PRIMJENU NA SLUZNICE

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UVOD I CILJ

Primjena lijeka putem sluznica tijela prepoznata je kao prikladna alternativa konvencionalnim putovima primjene, osiguravajući učinkovitiju lokalnu terapiju topikalnom primjenom te omogućujući sistemsku primjenu čime se izbjegava biorazgradnja lijeka tijekom prvog prolaska kroz jetru [1]. Velika raznolikost i kompleksnost dostupnih oblika te razlike u fizikalno-kemijskim svojstvima lijekova za (trans)mukoznu primjenu otvara nove izazove u ispitivanju njihove učinkovitosti. *In vitro* ispitivanje oslobađanja lijeka jedan je od osnovnih testova za karakterizaciju ljekovitog oblika u procesu razvoja nove formulacije te u osiguravanju i kontroli njegove kakvoće. Ovo predavanje daje sveobuhvatni pregled kompendijalnih i nekompendijalnih metoda za *in vitro* ispitivanje oslobađanja lijeka kod suvremenih oblika namijenjenih za primjenu lijeka na/putem sluznica tijela.

METODE

Podaci su sakupljeni korištenjem Scopus baze podataka, koristeći ključne riječi relevantne za područje istraživanja te uvidom u odgovarajuće monografije oficinalnih farmakopeja.

REZULTATI

Razvijene su i opisane različite aparature i testovi za *in vitro* ispitivanje oslobađanja lijeka iz (trans)mukoznih oblika. Pri tome se postavke ispitivanja, uključujući vrstu aparature, sastav i volumen receptorskog medija, karakteristike korištene membrane, brzinu miješanja i temperaturu pri kojoj se ispitivanje provodi prilagođavaju karakteristikama (trans)mukoznog oblika, fizikalno-kemijskim svojstvima djelatne tvari te uvjetima koji su prisutni na mjestu primjene. Ti parametri variraju u širokim rasponima i biti će detaljno opisani u ovom predavanju.

ZAKLJUČCI

U razvoju testa za *in vitro* oslobađanje djelatne tvari kao polaznu točku treba uzeti kompendijalne smjernice. Međutim, prisutna je potreba za razvojem i standardizacijom novih biorelevantnih testova, kao i uspostavljanje *in vitro*/*in vivo* korelacije, čime će se omogućiti bolja procjena učinka (trans)mukozne formulacije *in vivo*.

LITERATURA

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KLJUČNE RIJEČI: *in vitro* ispitivanje oslobađanja djelatne tvari, (trans)mukozni oblici

GUIDELINES FOR *IN VITRO* DRUG RELEASE TESTING IN CONTEMPORARY FORMS FOR ADMINISTRATION TO MUCOUS MEMBRANE

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INTRODUCTION AND OBJECTIVE

Administration of the drug via the mucous membranes of the body has been recognized as a suitable alternative to conventional methods of administration, providing more efficient local therapy through topical administration and enabling systemic administration to avoid drug biodegradation during first passage through the liver [1]. The wide variety and complexity of the forms available and the differences in the physicochemical properties of (trans) mucosal administration open new challenges in testing their efficiency. In vitro drug release testing is one of the basic tests for characterization of a drug form in the process of developing a new formulation and in ensuring and controlling its quality. This lecture provides a comprehensive overview of compendial and non-compendial methods for in vitro drug release testing in contemporary forms intended for drug administration to/through the mucous membranes of the body.

METHODS

Data were collected using the Scopus database, using keywords relevant to the research area, and insight into appropriate official pharmacopoeia monographs.

RESULTS

Various apparatus and tests have been developed and described for the in vitro drug release testing from (trans)mucosal forms. The test settings, including the type of apparatus, the composition and volume of the receptor medium, the characteristics of the membrane used, the mixing rate and temperature at which the test is carried out are adapted to the characteristics of the (trans)mucosal form, the physicochemical properties of the active substance and the conditions present at the place of application. These parameters vary over a wide range and they will be described in detail in this lecture.

CONCLUSIONS

Compendial guidelines should be taken as a starting point in the development of the *in vitro* drug release testing. However, there is a need to develop and standardize new biorelevant tests, as well as to establish *in vitro/ in vivo* correlations, thus allowing a better assessment of the effect of the (trans) mucosal formulation *in vivo*.

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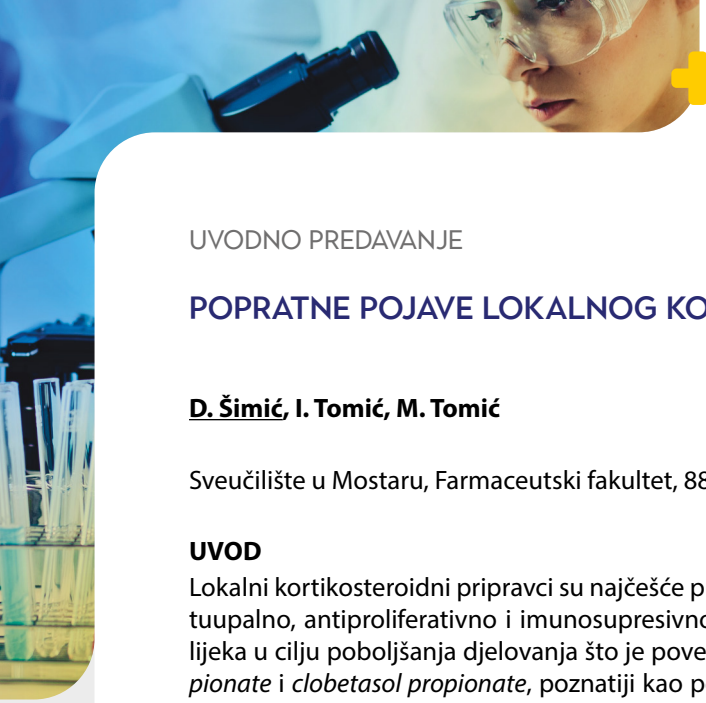
KEYWORDS: *in vitro* active substance release testing, (trans)mucosal forms



UVODNO PREDAVANJE

POPRATNE POJAVE LOKALNOG KORTIKOSTEROIDNOG LIJEČENJA

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UVOD

Lokalni kortikosteroidni pripravci su najčešće prepisivana terapija u liječenju dermatoloških bolesti. Imaju protuupalno, antiproliferativno i imunosupresivno djelovanje. Do danas su urađene modifikacije u potentnosti lijeka u cilju poboljšanja djelovanja što je povezano sa većim brojem popratnih pojava. *Betamethasone dipropionate* i *clobetasol propionate*, poznatiji kao peta generacija kortikosteroida, su primjeri potentnih molekula koje brzo poboljšavaju specifične dermatoze, ali su povezani sa nuspojavama koje se manifestiraju kao lokalne ili kao sistemske [1].

PREZENTACIJA SLUČAJEVA

Štetni utjecaji na koži posljedica su produženog liječenja, a ovise i o kemijskoj strukturi lijeka, vehiklu i osobito mjestu aplikacije lijeka. Popratne su pojave najučestalije vidljive na mjestu same aplikacije lijeka, a mogu se podijeliti u lokalne i sistemske nuspojave [2]. Lokalne su u današnje vrijeme učestalije. Manifestiraju se kao atrofija, strije, teleangiektazije, rozacea, perioralni dermatitis, akne, purpura, alergijske reakcije. Rijeđe su pojačana dlakavost, pigmentacije, odgođeno cijeljenje rana, egzacerbacija infekcija. Sistemske popratne pojave očituju se hiperglikemijom, glaukomom, opisani su slučajevi adrenalne insuficijencije kao posljedice dugotrajne primjene lokalnih pripravaka [3].

ZAKLJUČAK

Zbog toga je dermatolozima važno ispravno koristiti lokalne kortikosteroide znajući nuspojave te donijeti valjanu odluku o upotrebi primjereno bolesniku na temelju čimbenika kao što su dob, mjesto aplikacije i vrsta bolesti kože. Primjerena upotreba ovih lijekova uz suradnju bolesnika smanjuje rizik od nuspojava i može biti od velike koristi u liječenju dermatoloških bolesti.

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KLJUČNE RIJEČI: kortikosteroidi, lokalno liječenje, popratne pojave

SIDE EFFECTS OF TOPICAL CORTICOSTEROID THERAPY

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INTRODUCTION

Topical corticosteroids are the most commonly prescribed agents in the treatment of dermatologic conditions. They exhibit anti-inflammatory, anti-proliferative and immunosuppressive activities. Many structural modifications have been made to improve the efficacy of topical corticosteroids to produce drugs with greater potency, although this has often been associated with a higher likelihood of side effects. Betamethasone dipropionate and clobetasol propionate, known as fifth-generation corticosteroids, are a typical example of potent molecules that can control specific dermatoses very rapidly, but are associated with a high risk of topical and systemic side effects [1].

PRESENTATION OF CASES

Cutaneous adverse effects occur regularly with prolonged treatment and are dependent on the chemical nature of the drug, the vehicle, and the location of its application. The most common side effects are often manifested on application site. Side effects due to topical steroids can be divided into local side effects and systemic adverse effects [2]. Local side effects are more prevalent than systemic reactions. The most frequent adverse effects include atrophy, striae, telangiectasia, rosacea, perioral dermatitis, acne, purpura, allergic reactions. Those that occur with lower frequency include hypertrichosis, pigmentation alterations, delayed wound healing and exacerbation of skin infections. Problems related to systemic absorption, systemic reactions, such as hyperglycemia, glaucoma and adrenal insufficiency have also been reported to follow topical application [3].

CONCLUSION

This makes it important for us as dermatologists to weigh the usefulness of topical steroids versus their side effects, and to make an informed decision regarding their use in each individual case based on other factors such as age, site involved and type of skin disorder. Judicious use with reinforced patient education lowers such risk for side effects, and can be of great use in treating dermatologic conditions.

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KEY WORDS: corticosteroids, topical therapy, side effects

UVODNO PREDAVANJE

KAPSAICIN PODLOGA KAO SREDSTVO ZA BOLJU LOKALNU RESORPCIJU I DJELOVANJE LIJEKOVA

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UVOD I CILJEVI

Kapsaicin je alkaloid ljute paprike, kristalna supstanca bijele boje, bez mirisa. Ne rastvara se u vodi, ali se lako rastvara u alkoholu i uljima. Njegovo djelovanje na kožu izaziva osjećaj žarenja i hiperemije, jer pojačava cirkulaciju, omogućava postizanje i resorpciju lijekova na tretiranoj oblasti, kroz početnu depolarizaciju i oslobađanje neurotransmitera, također pomaže u ublažavanju reumatskog bola. Kapsaicin se koristi kao lokalni antireumatik i efikasan rubefacijens u lokalnim formulacijama u obliku tinktura, krema ili gelova, kao i u obliku flastera za primjenu na koži. Svrha ovog rada je analiza brzine resorpcije i sinergizam kapsaicina pripremljenog u obliku magistralne formulacije, kombinovan sa lijekovima za lokalnu primjenu.

METODE

Metod rada se zasniva na pripremi magistralnog preparata u različitim oblicima (gel, krema ili tinktura) sa određenim koncetracijama kapsaicina i lokalnih antireumatika, kapsaicina i dermatoloških lijekova, kapsaicina i sistemskih antireumatika.

REZULTATI

Kod dobrovoljaca ispitanika, bolesnika koji boluju od reumatoidnog artritisa, ispostavlja se da ovom kombinacijom kapsaicin ubrzava i pojačava djelovanje nesteroidnih antireumatskih lijekova za lokalnu upotrebu i lijekova za osteoporozu. Kod bolesnika sa određenom dermatološkom patologijom, podloga sa kapsaicinom povećava djelovanje dermatoloških lijekova na mjestu primjene. Imajući u vidu da kapsaicin povećava cirkulaciju krvi na mjestu primjene, omogućava da resorpcija i brzina djelovanja budu brži i sa druge strane jači, a kao rezultat povećanja cirkulacija na mjestu primjene i neurotransmiterskog djelovanja, koje posjeduje sam kapsaicin.

ZAKLJUČAK

Zasnivajući se na dobijenim rezultatima, možemo zaključiti da kapsacin zbog toga što povećava cirkulaciju krvi, omogućava bolju distribuciju lijeka na mjestu primjene. Stoga preporučujemo da se kod reumatskih bolesti i osteoporoze, kao i kod brojnih dermatoloških patologija, kao osnova za lijekove koristi kapsaicin u koncentracijama koje ne iritiraju kožu pacijenata na mjestu primjene.

KLJUČNE RIJEČI: kapsaicin, lokalni antireumatici, dermatološki lijekovi, magistralni preparati

CAPSAICIN BASE AS MEANS FOR BETTER LOCAL ABSORPTION AND EFFECT OF MEDICAMENTS

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INTRODUCTION
Capsaicin is an alkaloid of the spicy pepper, a white odorless crystal substance. It does not dissolve in water, but easily dissolves in alcohol and oils. Its effect on skin causes a burning feeling and hyperemia, because it boosts the blood flow, enables reaching and absorption of medicaments on the treated area, through initial depolarization and release of neurotransmitters, also helps soothe rheumatic pain. Capsaicin is administered as a local anti-rheumatic and efficient rubefacient in local formulations in the form of tinctures, creams or gels, as well as in the form of Band-Aids for on skin administration. The purpose of this study is to analyze the quickness of absorption and synergism of capsaicin prepared in the form of magistral formulation, combined with medicaments for local administration.

METHODS
The method of the study is based on preparation of the magistral preparation in various forms (gel, cream or tincture) with specific concentrations of capsaicin and anti-rheumatics, capsaicin and dermatological medicaments, capsaicin and system antirheumatics.

RESULTS
Providing that capsaicin enhances the blood flow on the location administered, it enables quick and resilient absorption and effectiveness and as a result of this enhancement of blood flow at the area administered and of neurotransmission effect, that capsaicin itself possesses.

CONCLUSION
Based on acquired results, we can conclude that capsaicin due to the fact that it enhances the blood flow; it enables better distribution of the medicament on the area administered. Therefore we recommend that capsaicin is used in rheumatic diseases and osteoporosis as well as in various dermatological pathologies as basis for medicaments in concentrations that do not irritate the skin of the patient on the area administered.

KEYWORDS: capsaicin, local anti-rheumatics, dermatological medicaments, magistral preparations.

ORALNA PREZENTACIJA

STRUKTUIRANJE 3D-PRINTANIH PLA MIKROIGALA ZA PREDTRETMAN TRANSDERMALNE DOSTAVE LIJEKOVA

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UVOD I CILJ

Iako mikroigle predstavljaju relativno novi sistem za dostavu lijekova, već se smatraju naprednim i efikasnim sistemima za poboljšanje transdermalnog transporta aktivnih supstanci [1]. Obzirom da je značajno da mikroigle budu efikasne i sigurne za upotrebu, bez neželjenih efekata, bez osjećaja boli i da imaju što jednostavniju primjenu, ovaj rad je fokusiran na struktuiranje mikroigala pomoću inovativne tehnologije 3D printanja i ispitivanje njihove fizičke stabilnosti.

METODE

Mikroigle različitih gustina (2x2, 3x3 i 5x5) te visina (0,6 mm; 1,2 mm i 1,8 mm) su dizajnirane koristeći Ultimaker Cura softver i isprintane pomoću 3D printera Ultimaker 5S (Ultimaker, Holandija) sa 0,6 mm PLA filamentom (Ultimaker, Holandija). Postavljeni su sljedeći parametri printanja: veličina vrha 0,25 mm; brzina printanja 30 mm/s; pri temperaturi od 180-210°C. Mikroigle su zašiljene procesom vlažnog nagrizanja u rastvoru NaOH (Sigma Aldrich) različitih koncentracija (1,5 M i 9 M). Fizička stabilnost ispitana je korištenjem hardness aparata TB24 (Erweka, Njemačka).

REZULTATI

Veća gustina (5x5) kao i veća visina (1,8 mm) rezultirala je preciznije isprintanim mikroiglama, bez stvaranja velikog otpadnog materijala između iglica. Različite koncentracije NaOH u procesu nagrizanja su utjecale na strukturu mikroigala, a najbolji rezultati su postignuti primjenom 5M NaOH u vremenu od 9 sati. Sve mikroigle, bez obzira na gustinu i visinu, izdržale su primjenu pritiska od preko 150 N bez lomljenja.

ZAKLJUČCI

Postavke printanja se mogu lako prilagoditi kako bi se razvile mikroigle optimalne gustine i visine. Zbog rezolucije printera, najbolji rezultati se postižu printanjem mikroigala veće gustine i visine. Proces nagrizanja omogućava reduciranje debljine mikroigala što utiče na lakšu penetraciju kroz *stratum corneum*. Obzirom da je sila potrebna za penetraciju niza mikroigala površine 1 cm^2 0,1 – 3 N, mikroigle dobivene tehnikom 3D printanja pokazale su izvrsnu fizičku stabilnost, te prilikom aplikacije neće doći do loma igala, što znači da se ovako struktuisane mikroigle mogu uspješno koristiti za predtretman transdermalne dostave lijekova.

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KLJUČNE RIJEČI: mikroigle, 3D printanje, transdermalna dostava lijekova

STRUCTURING OF 3D-PRINTED PLA MICRONEEDLES FOR PRE-TREATMENT OF TRANSDERMAL DRUG DELIVERY

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INTRODUCTION AND OBJECTIVE

Although microneedles present a relatively new drug delivery system, they are already considered to be an advanced and effective system for improved transport of active pharmaceutical ingredients for transdermal delivery [1]. As it is essential for delivery to be effective, pain-free, safe to use, without side effects and to have application as simple as a possible, this paper focuses on structuring microneedles using innovative 3D-printing technology and on examining their physical stability.

METHODS

Microneedles with different densities (2x2, 3x3 and 5x5) and heights (0.6 mm; 1.2 mm and 1.8 mm) were designed using Ultimaker Cura software and printed by Ultimaker 5S 3D printer (Ultimaker, Netherlands) with 0.6 mm PLA filament (Ultimaker, Netherlands). The following print parameters were set up: tip size 0.25 mm; print speed 30 mm/s at 180-210°C. Microneedles were etched using the wet etching process in a NaOH solution (Sigma Aldrich) with different concentrations (1, 5 M and 9 M). Physical stability was tested using hardness apparatus TB24 (Erweka, Germany).

RESULTS

Higher density (5x5) and height (1.8 mm) resulted in more accurately printed microneedles without a lot of waste material between the needles. Different concentrations of NaOH in the etching process affected the structure of the microneedles. The best result was achieved with 5 M NaOH over a time of 9 hours. All microneedles, regardless of their density and height, have withstood a pressure of over 150 N without breaking.

CONCLUSIONS

Printing parameters can easily be adjusted to develop microneedles of optimal density and height. Due to the printer resolution, the best results are achieved by printing microneedles with higher density and height. The etching process, which reduces the thickness of the microneedles, results with easier penetration through *stratum corneum*. Considering that the required penetration force of a series of microneedles with a surface area of 1 cm^2 is 0.1-3 N, 3D printed microneedles have shown excellent physical stability, since they will not break during the administration, meaning that such structured microneedles can be employed for the pre-treatment of transdermal drug delivery.

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KEYWORDS: microneedles, 3D printing, transdermal drug delivery

ORALNA PREZENTACIJA

ODREĐIVANJE SADRŽAJA RANITIDIN HIDROHLORIDA HPLC-METODOM I STABILNOSTI MAGISTRALNO PRIPREMLJENOG RANITIDIN SIRUPA

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UVOD I CILJ

Ranitidin je antagonist histaminskih H2-receptora. Ima mnogo indikacija uključujući bolest gastroezofagealnog refluksa, te se koristi u profilaksi ulceracija uslijed stresa kod teško bolesnih pacijenata [1]. Ranitidin hidrohlorid je fotosenzitivna supstanca i stoga se sama supstanca kao i njezini ljekoviti oblici moraju čuvati u zatamnjenoj ambalaži koja štiti od fotodegradacije [2]. Na tržištu BiH ne postoji registriran gotov preparat u obliku sirupa, te se u bolničkoj apoteci Univerzitetsko kliničkog centra u Tuzli, za potrebe pedijatrijskih pacijenata priprema magistralni pripravak. Cilj je ispitati stabilnost magistralno izrađenog pripravka korištenjem HPLC metode.

METODE

Pripremljen je sirup otapanjem ranitidin hidrohlorida u otopini: voda:sirup simpleks (30:70) u koncentraciji od 20 mg/mL. U cilju ispitivanja stabilnosti sirup se čuva u uvjetima (25˚C 60% vlažnosti / 40˚C 75% vlažnosti) i izlaže djelovanju dnevne svjetlosti (D65 standard prema ISO 2470-2:2008). Sadržaj ranitidin hidrohlorida se određuje HPLC metodom koja je za potrebe ispitivanja validirana. Kalibraciona kriva je pokazala linearnost u ispitivanom koncentracijskom opsegu od 23, 07 µg/ml do 138,43 µg/ml ($y = 34461x + 408179$; $R_2 = 0,9911$).

REZULTATI

Zabilježeno je kratko trajanje analize (RT 4,707 min) i dobra ponoljivost praćenih parametara (RSD za RT:1,02 % i A: 0,987 %).

ZAKLJUČCI

Odabrana HPLC metoda za određivanje sadržaja ranitidin hidrohlorida u sirupu je pogodna za rutinsku analizu zbog kratkog trajanja analize i dobre ponovljivosti praćenih parametara.

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KLJUČNE RIJEČI: ranitidin hidrohlorid, HPLC, sirup, fotodegradacija

STABILITY AND CONTENT DETERMINATION OF RANITIDINE HYDROCHLORIDE IN MAGISTRAL SYRUP PREPARATION BY HPLC

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OBJECTIVES

Ranitidine is a histamine H2-receptor antagonist that acts by antagonizing histamine at gastric H2-receptor sites. Ranitidine is used for many different indications including gastroesophafgeal reflux disease and the prophylaxis of stress ulceration in critically ill patients [1]. Ranitidine hydrochloride and it's pharmaceutical preparations need to be stored in brown glass package protected from light and photodegradation because it's photosensitive [2]. In BiH there's no registrated pharmaceutical preparation of ranitidine hydrochloride in form of syrup. In hospital pharmacy of UKC Tuzla magistral formulation of ranitidine hydrochloride is made in form of syrup for pediatric patients on daily basis.

The goal is to examine stability of magistral preparation – ranitidine hydrochloride syrup using the HPLC method.

METHODS

Ranitidine hydrochloride was disolved in water in order to prepare oral syrup in proportion: water : simplex syrup (30 : 70) in concentration of 20 mg/mL. For stability studies syrup is stored under the various storage conditions (25˚C 60% humidity / 40˚C 75% humidity) and exposed to daylight (D65; ISO 2470-2:2008). HPLC method is used to determine content of ranitidine hydrochloride in syrup. This method is validated and calibration curve has shown linearity in tested calibration range from 23, 07 µg/mL to 138,43 µg/mL ($y = 34461x + 408179$; $R_2 = 0,9911$).

RESULTS

It's been noted that analysis requires short period of time for anlysing (RT 4,707 min) while showing good reproducibility of tested parameters (RSD for RT:1,02 % and A: 0,987 %).

CONCLUSIONS

The chosen HPLC method for the determination of ranitidine hydrochloride in oral syrup resulted suitable as routine analysis due to short anlysing period and good reproducibility of monitored parameteres.

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KEY WORDS: ranitidine hydrochloride, HPLC, syrup, photodegradation

ORALNA PREZENTACIJA

FORMULAB: FORMULIRANJE PREPARATA ZA NJEGU KOŽE

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UVOD I CILJ

Magistri farmacije su osposobljeni nakon završetka studija Farmacije da izrađuju farmaceutske preparate. Međutim, kreiranje novih preparata, naročito kozmetičkih, zahtjeva dodatnu edukaciju, kako bi se formuliranju pristupilo na sistematičan i ekonomičan način.

Iako je kozmetička industrija u svijetu razvijena i profitabilna, u Bosni i Hercegovini ona čini tek vrlo mali udio ukupne proizvodnje. Trenutno kozmetičke preparate proizvodi mali broj malih i mikro preduzeća, ali određene iskorake također čine i apoteke i galenski laboratoriji. U ovakvim firmama leži potencijal za velikim rastom i povećanom konkurentnosti ukoliko bi koristili nove materijale i tehnike, te kreativniji pristup formuliranju kozmetičkih preparata.

Cilj programa cjeloživotnog učenja „Formulab: formuliranje preparata za njegu kože“ na Farmaceutskom fakultetu Univerziteta u Sarajevu je osposobiti polaznike za veći zamah formuliranja kozmetike za njegu kože, a u cilju kreiranja vlastitih proizvoda. Ovaj program daje mogućnost praktičnog upoznavanja sa širokom paletom materijala (kozmetičkih aktivnih supstanci, emulgatora, masnih faza, reoloških modifikatora, antioksidanasa, konzervanasa, mirisa), koji se koriste u kozmetičkim preparatima. Program nudi nova saznanja o načinima rukovanja sa pojedinim sastojcima, te načinima izrade preparata za njegu, sa naročitim akcentom na emulzijske preparate (kreme, losioni, gelovi, masti, voskovi). Budući da se formulator oslanja na prethodna stručna i naučna dostignuća i iskustva, kroz program se osposobljava da sistematično analizira i kopira sastav formulacije već prisutne na tržištu (deformuliranje ili reverzni inženjering), što na kraju i praktično pokazuje. Također, uočava i nedostatke tih formulacija, te daje rješenja za njihovo poboljšanje ili zamjene pojedinih sastojaka uz potvrdu svojih razmišljanja praktičnim radom. Naročit je akcent na praktični rad (“*hands on*” pristup), te razvijanje kreativnosti pri formuliranju novih preparata, kroz Formulatorski poligon. Rad se odvija u malim grupama (maksimalno 15 polaznika), a dvije trećine časova odvija se kroz praktičnu nastavu.

Po uspješnom završetku programa učesnici dobivaju certifikat, a edukacija je bodovana od strane Farmaceutske komore Federacije BiH.

KLJUČNE RIJEČI: cjeloživotno učenje, formuliranje, kozmetika za njegu kože.

FORMULAB: FORMULATING SKIN CARE PRODUCTS

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INTRODUCTION AND OBJECTIVE

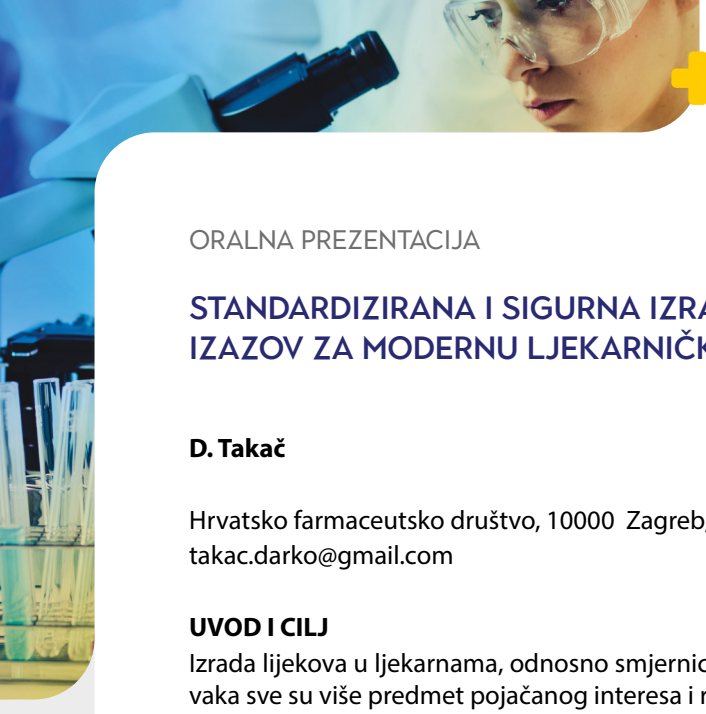
The masters of pharmacy are trained after the completion of their pharmacy studies to manufacture pharmaceutical preparations. However, the creation of new preparations, especially cosmetic ones, requires additional training in order to approach formulating in a systematic and economical way.

Although the cosmetic industry in the world is developed and profitable, in Bosnia and Herzegovina it accounts for only a very small share of total production. Currently, cosmetic products are manufactured by a small number of small and micro businesses, but pharmacy and galenic laboratories are also making some strides. Such companies have the potential for great growth and increased competitiveness if new materials and techniques are used, as well as a more creative approach to formulating cosmetic products.

The aim of the lifelong learning program "Formulab: Formulating Skin Care Products" at the Faculty of Pharmacy, University of Sarajevo is to empower students to take more momentum in formulating of skin care cosmetics in order to create their own products. This program gives the opportunity to familiarize with a wide variety of materials (cosmetic active substances, emulsifiers, oily phases, rheological modifiers, antioxidants, preservatives, fragrances) used in cosmetic preparations. The program offers new insights into handling of individual ingredients and manufacturing skin care products, with particular emphasis on emulsion products (creams, lotions, gels, ointments, waxes). Because the formulator draws on previous professional and scientific achievements and experience, the program enables students to systematically analyze and copy the composition of a formulation already present on the market (deformation or reverse engineering), which they practically show at the end. It also enables students to recognize the drawbacks of present formulations, and provide solutions for improving them or replacing particular ingredients while validating their thinking through practical work. Emphasis is placed on hands-on approach and the development of creativity in formulating new preparations through the Formulator Polygon. The work is carried out in small groups (maximum 15 students), and two thirds of the classes take place through practical excercises.

Upon successful completion of the program, participants receive a certificate and the education is scored by the Federation of B&H Pharmaceutical Chamber.

KEYWORDS: lifelong learning, formulation, skin care cosmetics.



ORALNA PREZENTACIJA

STANDARDIZIRANA I SIGURNA IZRADA MAGISTRALNIH I GALENSKIH LIJEKOVA – IZAZOV ZA MODERNU LJEKARNIČKU PRAKSU I REGULATIVU U HRVATSKOJ

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UVOD I CILJ

Izrada lijekova u ljekarnama, odnosno smjernice i standardi te dokazi sigurnosti izrade i djelotvornosti pripravaka sve su više predmet pojačanog interesa i rasprava u farmaceutskim i regulatornim institucijama te zdravstvenoj javnosti. Razlozi su prvenstveno: veća prava i sigurnost pacijenta, transparentni indikatori kvalitete zdravstvenih intervencija, harmonizacija zdravstvenih usluga u Europi te sustavna evaluacija ishoda farmakoterapije. Moderni trendovi u razvoju magistralnih i galenskih lijekova/pripravaka te bolja dostupnosti novih farmaceutskih oblika, farmaceutskih tvari i aplikacijskih sustava uvjetuju kvalitetniju standardizaciju prakse i regulative [1]. Stvara se i novo paradigma farmakoterapije - personalizirana priprema doze i formulacije lijeka za ciljanu/preciznu terapiju pacijenta ili vrlo male skupine pacijenata. Cilj je prikazati glavne značajke i rezultate na dokazima utemeljene magistralne i galenske farmacije, te hrvatski regulatorni okvir za to područje.

METODE I REZULTATI

Kvalificirana i standardizirana izrada pripravaka zahtjeva nova i specifična znanja i vještine ljekarnika, profesionalnu opremljenost te validirane laboratorijske postupke i prostore za izradu različitih oblika. Značajan broj rizičnih faktora nepovoljno utječu na izradu i sustav osiguranja/upravljanja kvalitetom. Faktori su: specifikacije sastavnica, farmaceutski izračun, reference doziranja i stabilnost pripravka, inkompatibilnost tvari, kontaminacija, postupak oblikovanja i dr. Dio nesukladnosti potencira: ulazna kvaliteta tvari, neadekvatan prostor, oprema te razina edukacije i kompetencija stručnog osoblja, način čuvanja i stabilitet pripravka, označavanje i prateća farmaceutska dokumentacija [2]. Dobra regulatorna praksa, organizacija rada i uspostavljeni sustav osiguranja/upravljanja kvalitetom temeljni su uvjeti za modernu i sigurnu izradu pripravaka. Usvajanjem *Resolution CM/ResAP (2011)1* Vijeća Europe ostvaren je poticaj za bolje zakonsko reguliranje u Hrvatskoj [3].

ZAKLJUČCI

Bez obzira na načelnu spremnost ljekarnika da preuzmu svoju staru/novu ulogu izrade lijekova, dio ljekarni neće biti u mogućnosti stručno odgovoriti tim izazovima. Samo specijalizirane ljekarne s adekvatnim kadrom, opremom i prostorom te GMP sustavom osiguranja/upravljanja kvalitetom mogu biti nositelji tog ljekarničkog sadržaja. Promiđbom izvrsnosti struke i pripravaka te interdisciplinarnom suradnjom u zdravstvu povećati će se propisivanje i terapijska upotreba pripravaka.

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KLJUČNE RIJEČI: magistralni i galenski lijekovi, izrada, regulativa

STANDARDIZED AND SAFE COMPOUNDING OF MAGISTRAL AND GALENIC DRUGS - A CHALLENGE TO MODERN PHARMACEUTICAL PRACTICE AND REGULATION IN CROATIA

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INTRODUCTION AND OBJECTIVE

Drug compounding in pharmacies, its guidelines and standards, and evidence of the production safety and efficacy of the preparations, are increasingly becoming the subject of interest and debate in pharmaceutical and regulatory institutions and the healthcare system. The primary reasons are greater patients' rights and safety, transparent indicators of the quality of health interventions, harmonization of health services in Europe, and systematic evaluation of pharmacotherapy outcomes. Modern trends in the development of magistral and galenic preparations as well as better availability of new pharmaceutical forms, pharmaceutical substances and application systems require better standardization of practice and regulation [1]. A new paradigm for pharmacotherapy is being created - personalized dose preparation and drug formulations for targeted/accurate therapy of a patient or a very small group of patients. The aim of this paper is to present the main features and results of evidence-based magistral and galenic pharmacy, as well as the Croatian regulatory framework for this area.

METHODS AND RESULTS

Qualified and standardized preparation of pharmacy products requires a new specific knowledge and skills of pharmacists, professional equipment and validated laboratory procedures and facilities for the production of various formulations. A number of risk factors have an adverse effect on the design and the quality assurance/management system. Risk factors include ingredient specifications, pharmaceutical calculations, dosage references and stability of preparation, substance incompatibility, contamination, design process, etc. Part of the non-compliance is potentiated by the quality of the input substance, inadequate space, equipment, level of education and competence of professional staff, storage method and stability preparation, labeling and the supporting pharmaceutical documentation [2]. Good regulatory practice, work organization and an established quality assurance/quality management system are the basic conditions for modern and safe pharmaceutical preparation of products. Incentive for better regulation was achieved by adoption of the *Council* of *Europe Resolution CM*/ResAP (2011) 1 [3].

CONCLUSIONS

Regardless of the pharmacists' readiness to take on their old/new role in drug preparation, some pharmacies will not be able to meet these professional challenges. Only specialized pharmacies with adequate staff, equipment and facilities and GMP quality assurance/quality management systems may adopt this pharmacy content. The prescribing and therapeutic application of these preparations will be enhanced by promoting the excellence of the profession and the quality of the preparations as well as by interdisciplinary collaboration in the healthcare system.

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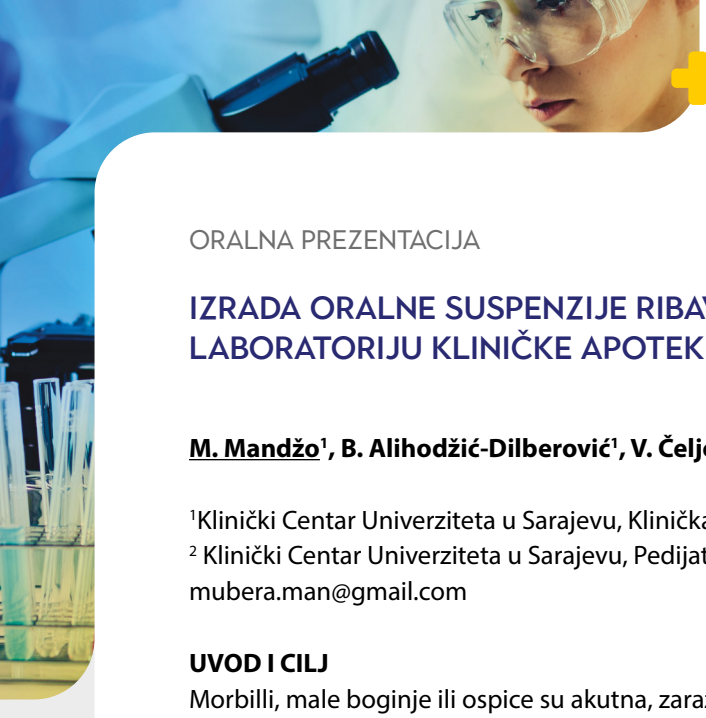
KEY WORDS: magistral and galenic medicines (drugs), compounding, regulation



ORALNA PREZENTACIJA

IZRADA ORALNE SUSPENZIJE RIBAVIRINA 40 mg/mL U GALENSKOM LABORATORIJU KLINIČKE APOTEKE KCU SARAJEVO ZA MORBILLE KOD DJECE

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UVOD I CILJ

Morbilli, male boginje ili ospice su akutna, zarazna virusna bolest koja se vrlo lako širi. Uzročnik bolesti je virus morbila koji se prenosi kapljičnim putem, kontaktom s bolesnikom, njegovim sekretima iz usta i nosa kao i preko kontaminiranih predmeta. Komplikacije uključuju proljev, upalu uha, pluća ,mozga i smrt. Cilj rada jeste prikazati neophodnost i značaj Galenskog laboratorija u Kliničkoj apoteci KCU–Sarajevo, posebno u slučajevima kada potrebni lijek nije dostupan na našem tržištu. Izradom oralne suspenzije Ribavirina 40 mg/mL obezbijedili smo oboljeloj djeci efikasan, bezbijedan i kvalitetan lijek. Izrađenu oralnu suspenziju su koristila djeca do jedne godine starosne dobi hospitalizirana na Pedijatrijskoj klinici.

METODE

Djeca kod kojih su se javile morbille primala su Ribavirin oralnu suspenziju 40 mg/mL koja se pripremila u Galenskom laboratoriju. Oralna suspenzija se davala per os, odnosno putem nazogastrične sonde, po potrebi, dva puta na dan djeci u Jedinici pedijatrijske intenzivne njege. Za izradu oralne suspenzije Ribavirina koristili smo Ribavirin caps. 200 mg i vehikulum Ora-Sweet. Potrebnu količinu Ribavirin caps. smo otvorili u tarioniku, dobiveni prašak miješali sa Ora-Sweetom 15 minuta sve do nastanka jednakomjerne glatke suspenzije. Dobivenu suspenziju smo prebacili u tamnu staklenu bočicu, još jednom dobro promiješali i signirali.

REZULTATI

Djeca koja su primala suspenziju Ribavirina bila su 4 pacijenta u skupini od 0-6 mjeseci i 5 pacijenata u skupini od 6-12 mjeseci. U obe grupi (do 1 god) bilo je 4 pacijenta sa komorbiditetima od kojih je 2 djece bilo na mehaničkoj ventilaciji, 1 je imalo miokarditis, 1 komplikacije CNS, a 1 od te djece je egzitiralo. Ukupno u ovoj grupi do 1 godine bilo je 3 djece na mehaničkoj ventilaciji, 2 sa miokarditisom i 1 sa komplikacijama CNS. Liječenje morbilla je simptomatsko (ublažavanje simptoma) i trajalo je sve dok djeca nisu bila bez znakova morbilla.

ZAKLJUČCI

Propisivanje magistralnih pripravaka u kliničkoj praksi je sve češće obzirom da se doziranje lijeka individualno prilagođava svakom pacijentu. Magistralni pripravci imaju značajno mjesto u terapiji i liječenju, posebno u slučajevima kada određeni lijek nije dostupan na domaćem tržištu.

KLJUČNE RIJEČI: morbille,oralne suspenzije,ribavirin

PREPARATION OF RIBAVIRINE 40 mg/mL ORAL SUSPENSION FOR MORBILLES IN CHILDREN IN THE GALENIC LABORATORY OF THE CLINICAL PHARMACY OF THE UNIVERSITY OF SARAJEVO CLINICAL CENTRE

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INTRODUCTION AND OBJECTIVE
Morbilli or measles is an acute infectious viral disease that is easily spread. The disease is caused by a measles virus transmitted by droplet contacts, contact with patients, mouth and nose secretions, including contaminated objects. Possible complications include diarrhoea, ear infections, pneumonia, encephalitis and death. Objective of this paper is to demonstrate the necessity and importance of having the Galenic Laboratory within the Clinical Pharmacy of the Clinical Centre of the University of Sarajevo, especially in cases when the required medication is not available on our market. By preparing the Ribavirin 40 mg/mL oral suspension we have provided the infected children with an effective, safe and high-quality medication. The oral suspension was given to children up to one year of age, hospitalised at the Paediatric Clinic.

METHODS
Children with measles received Ribavirin 40 mg/mL oral suspension prepared at the Galenic Laboratory. The suspension was administrated *per os*, that is through a nasogastric tube, as needed, two times a day, to children hospitalised at the Paediatric intensive care unit. For the preparation of the Ribavirin oral suspension we used Ribavirin caps. 200 mg and Ora-Sweet vehiculum. The required amount of Ribavirin caps. was opened in a mortar and the obtained powder was mixed with Ora-Sweet for 15 minutes until a uniform, smooth suspension was formed. The obtained suspension was then moved to a dark glass bottle, once again stirred and signified.

RESULTS
Children receiving Ribavirin suspension were divided in two groups according to their age: 0-6 months - 4 patients and 6-12 months - 5 patients. In both groups (children aged up to 1 year) there were 4 patients with comorbidities, of which 2 children on mechanical ventilation, 1 with myocarditis, 1 experiencing CNS complications and 1 of these children died. In this group of up to 1-year old children there were in total 3 children on mechanical ventilation, 2 with myocarditis and 1 with CNS complications. Measles treatment was symptomatic (relieving symptoms) and lasted until the children had no signs of measles.

CONCLUSIONS
Prescription of magisterial medications in clinical practice is becoming increasingly common as the dosage is adapted to the individual needs of each patient. Magistral medications have a significant place in therapy and treatment, especially in cases when a certain medication is not available on the domestic market.

KEY WORDS
Morbilli, oral suspension, ribavirin

POSTER

ANTITUMORSKA AKTIVNOST ČVRSTIH LIPIDNIH NANOČESTICA SA RESERVATOLOM

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UVOD I CILJ

Resveratrol se definira kao (3,5,4'-trihidroksi-trans-stilben), a klasificira se kao prirodni polifenol koji se sastoji od dva fenolska prstena koji su spojeni metilenskim mostom. Ovaj aktivni spoj pokazao je snažnu pleiotropsku, antineoplastičnu aktivnost bez dokumentirane toksičnosti za normalne ćelije. Pored toga, brojne studije su navele da resveratrol, kao najistraženiji stilben, posjeduje brojne zdravstveno korisne karakteristike, kardioprotektivnost, antidijabetičnost, neuroprotektivnost i kemopreventivnost. Nažalost, klinička upotreba resveratrola je ograničena zbog njegove niske topivosti u vodi (0,05 mg/mL), razgradnji na fiziološkom pH koji je povezan s ekstremno niskom sistemskom biodostupnosti. Intrigantna strategija za prevazilaženje ovih ograničenja je formuliranje nanočestica s reservatrolom kao što su čvrste lipidne nanočestice kao platforme za prenos do ciljnih tkiva.

METODE

U svrhu istraživanja izvršili smo detaljan pregled podataka iz kliničkih studija različitih formulacija čvrstih lipidnih nanočestica s resveratrolom, procesa pripreme i karakterizacije njihove strukture, obradili utjecaj različitih parametara na stabilnost, a patentirane formulacije koje se stavljaju na tržište smo popisali. Podatke smo dobili pretragom odgovarajuće naučne, stručne literature, ukazali smo na prednosti i nedostatke nanočestica i diskutirali o rezultatima kliničkih studija čvrstih lipidnih nanočestica s resveratrolom.

REZULTATI

Dobijeni rezultati pokazali su značajno poboljšanu bioraspoloživost i stabilnost resveratrola ugrađenog u čvrste lipidne nanočestice (SLN). Naprimjer, intravenska primjena SLN-a s resveratrolom na štakorima pokazala je citotoksičnost na ćelijama C6 glioma i značajno poboljšala ćelijsku internalizaciju. Ispitana je i raspodjela u mozgu, a rezultati su pokazali značajno veću koncentraciju SLN-a s resveratrolom, čak devet puta, u poređenju sa slobodnom otopinom hidrofobnog lijeka.

ZAKLJUČCI

Nanočestice s resveratrolom pokazale su izvanredne prednosti u odnosu na nekapsulirani agens. Problemi s niskom topivosti, niskom sistemskom cirkulacijom i stabilnošću značajno su poboljšani ugradnjom ovog djelotvornog sredstva u nanočestice.

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KLJUČNE RIJEČI: resveratrol, cilj, tumor, čvrste lipidne nanočestice

ANTITUMOR ACTIVITY OF RESVERATROL LOADED SOLID LIPID NANOPARTICLES

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INTRODUCTION AND OBJECTIVE

Resveratrol is identified as (3,5,4'-trihydroxy-trans-stilbene), classified as natural polyphenol consisting of two phenolic rings attached by methylene bridge. This active compound exhibited potent pleiotropic, antineoplastic activity without documented toxicity to normal cells. In addition, numerous studies reported that resveratrol, as most researched stilbene, possess numerous health-benefitial properties, such as cardioprotective, antidiabetic, neu-roprotective and chemopreventive. Regretfully, clinical use of resveratrol is restricted due to its poor aqueous solubility (0.05 mg/mL), degradation at physiological pH associated with extremely low systemic bioavailability. An intriguing strategy to overcome these limitations is formulation of resveratrol-loaded nanoparticles such as solid-lipid nanoparticles as platforms for delivery to target tissues.

METHODS

For the purpose, we did a detailed overview of data from clinical studies of various formulations of resveratrol loaded solid lipid nanoparticles, process of preparation and characterization of their structure, influence of various parameters on stability are processed and the patented formulations placed on the market are listed. We obtained the data by searching a relevant scientific-professional literature, we pointed out the advantages and disadvantages of the nanoparticles and discussed the results of clinical studies of resveratrol loaded solid lipid nanoparticles.

RESULTS

Obtained results showed significantly improved bioavailability and stability of resveratrol incorporated into solid-lipid nanoparticles (SLN). For example, intravenous application of resveratrol loaded SLN in rats showed cytotoxicity on C6 glioma cells and significantly improved cell internalization. Brain distribution was also tested and results showed substantially higher concentration, even nine folds, of resveratrol loaded SLN compared with free solution of the hydrophobic drug.

CONCLUSIONS

Resveratrol loaded nanoparticles showed remarkable advantages over non-encapsulated agent. Low-solubility problems, low systemic circulation and stability were significantly improved with encapsulation of this efficacious agent into nanoparticles.

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KEY WORDS: resveratrol, target, tumor, solid lipid nanoparticles

POSTER

PERSONALIZIRANE I 3D PRINTANE TABLETE: PREDNOSTI U ODNOSU NA KONVENCIONALNE FARMACEUTSKE OBLIKE

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UVOD I CILJ

3D printane tablete su kompleksni farmaceutski oblici malih dimenzija. Ovi 3D-objekti izrađeni su iz digitalnog modela, a njihove se željene karakteristike formiraju pomoću kompjuterskih programa. Cilj ovog rada bio je prikazati koje su prednosti ovog farmaceutskog oblika u odnosu na već postojeće, konvencionalne oblike.

METODE

Proučene su i upoređene studije koje se bave ovom tematikom. Tip istraživanja bio je deskriptivni i retrospektivni. Kao izvori informacija korišteni su originalni članci objavljeni u medicinskim časopisima i baze podataka Medline i Google Scholar.

REZULTATI

3D tablete pokazuju vrlo dobre performanse u pogledu reproducibilnosti, tačnosti doziranja i preciznosti kontrole željenih profila oslobađanja. Mogu se koristiti za izradu personaliziranih lijekova, što je značajno kod primjene lijekova sa uskim terapijskim indeksom i onih čija farmakokinetika bitno ovisi o genetskim polimorfizmima. Višeslojne 3D tablete pružaju mogućnost smanjenja intervala doziranja čime se znatno poboljšava adherenca pacijenata [1].

Izrađuju se aditivnim proizvodnim procesom zbog čega mogu imati specifičan prostorni raspored više različitih ljekovitih supstanci. To nadalje nudi potencijal za primjenu sistema sa kontinuiranim, vremenski kontrolisanim ili ciljanim profilima oslobađanja, kao i kombinovanje više ovakvih sistema. Omogućeno je i povećanje rastvorljivosti slabo rastvorljivih aktivnih supstanci te kombinovanje inkompatibilnih supstanci. U izradi se koriste porozni materijali koji omogućavaju brzo ostvarivanje terapijskog efekta [2].

Proizvodni proces je podesiv, fleksibilan i brz. Reducirana je upotreba pomoćnih supstanci, količina otpadnog materijala i vrijeme trajanja proizvodnog procesa što rezultira smanjenjem ukupnih troškova proizvodnje [3].

ZAKLJUČCI

Glavne prednosti 3D tableta u odnosnu na konvencionalne oblike su produkcija malih količina ljekovitih oblika od kojih svaki može imati prilagođenu dozu, oblik, veličinu i karakteristike oslobađanja aktivne supstance, mogućnost personaliziranja terapije te prostorno kontrolisanje pohranjivanja više ljekovitih supstanci sa varijacijama poroziteta i strateško pozicioniranje matriksa.

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KLJUČNE RIJEČI

3D printanje, 3D tablete, profil oslobađanja

PERSONALISED AND 3D-PRINTED TABLETS: ADVANTAGES OVER CONVENTIONAL PHARMACEUTICAL FORMS

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INTRODUCTION AND OBJECTIVE

3D-printed tablets are complex pharmaceutical forms small in dimension. These 3D-objects are fabricated from a digital model, and their desired characteristics are formed using computer-aided design software. This paper aimed to outline the benefits of this pharmaceutical form over the existing conventional forms.

METHODS

Studies dealing with this issue are examined and compared. The type of research was descriptive and retrospective. Original articles published in medical journals, as well as Medline and Google Scholar databases, were used as sources of information.

RESULTS

3D-printed tablets show excellent performance in terms of reproducibility, dosing accuracy, and precise control of desired release profiles. The possibility of their use as personalized medicine is significant for drugs with a narrow therapeutic index and those whose pharmacokinetics are significantly dependent on genetic polymorphisms. Multilayer 3D-tablets offer the ability to reduce the dosage interval, significantly improving patients adherence [1].

Because 3D-printed tablets are fabricated using an additive manufacturing process, they can have a specific spatial arrangement of different active pharmaceutical ingredients (APIs). Systems with continuous, time-controlled or target release profiles, as well as a combination of such systems, can be applied using this technology. It is also possible to improve the solubility of poorly soluble APIs and to combine incompatible substances. The porous materials used in the production process enable the therapeutic effect to be achieved quickly [2].

The manufacturing process is adjustable, flexible, and fast. The decrease in the total manufacturing cost is achieved using this technology by reducing the use of excipients, the amount of waste material, and the duration of the production process [3].

CONCLUSIONS

The main advantage of 3D-printed tablets over conventional pharmaceutical forms is the production of small quantities of medicines, each of which may have customized dosage, shape, size, and API release characteristics. Furthermore, it is possible to personalize therapy and to spatially control the storage of multiple APIs with variations in porosity and strategic matrix positioning.

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KEYWORDS

3D printing, 3D–printed tablets, release profile

POSTER

NANOEMULZIJE KAO SISTEMI ZA CILJANU DOSTAVU LIJEKOVA

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UVOD I CILJ

Nanoemulzije su termodinamički stabilni, izotropni sistemi dvije tečnosti koje se ne miješaju i odgovarajućeg surfaktanta. Lijekovi ili biomolekule su inkorporirani u unutrašnju strukturu nanoemulzija ili adsorbirani na njihovoj vanjskoj površini. Nanoemulzije karakteriše fizička i biološka stabilnost, dobra podnošljivost komponenti te mogućnost sterilizacije i liofilizacije. Proizvodnja im je relativno jednostavna i jeftina. Sve navedeno ih čini pogodnim za formulisanje oblika sa ciljanim oslobađanjem ljekovite supstance te je njihovo formulisanje, karakterizacija i potencijalna aplikacija u fokusu velikog broja istraživanja.

METODE

Proučene su i upoređene studije koje se bave ovom tematikom. Tip istraživanja bio je deskriptivni i retrospektivni. Kao izvori informacija korišteni su originalni članci objavljeni u medicinskim časopisima i baze podataka Medline i Google Scholar.

REZULTATI

Nanoemulzije značajno poboljšavaju bioraspoloživost oralno primijenjenih lijekova, uključujući i proteine, peptide i hidrofobne molekule. Surfaktanti koji se nalaze u sastavu nanoemulzija induciraju membransku protočnost i povećavaju permeabilnost što poboljštava apsorpciju, povećava rastvorljivost i reducira enzimatsku hidrolizu [1].

Radi postizanja optimalne bioraspoloživosti i minimalne iritacije prilikom dermalne i transdermalne aplikacije, nanoemulzije sadrže pojačivače penetracije koji fluidiziraju lipidni dvosloj *stratum corneum-a* i tako povećavaju permeaciju [2].

Nanoemulzije se mogu primijenjivati i u tretmanu određenih moždanih poremećaja jer uspješno zaobilaze retikulo-endotelni sistem krvno-moždane barijere. Nanoemulzije u obliku nazalnih sprejeva pružaju dobre mogućnosti za ciljanu dostavu lijekova u mozak kod kliničkih stanja koja zahtijevaju brzo ostvarivanje terapijskog efekta [3].

ZAKLJUČCI

Nanoemulzije imaju brojne prednosti u odnosu na konvencionalne ljekovite oblike. Imaju dobru sposobnost penetracije u ćelije i tkiva pri čemu dospijevaju u ciljane organe. Zbog svoje male veličine mogu biti transportovane kroz kapilare, izbjegavajući fagocitozu te imaju produžen protok u sistemskoj cirkulaciji. Poboljšavaju efikasnost i stabilnost lijekova i reduciraju njihove toksične efekte. Biorazgradivost nanoemulzija, te njihova osjetljivost na temperaturu i pH vrijednost može se iskoristiti za prilagođavanje kontrolisanog oslobađanja lijekova.

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KLJUČNE RIJEČI: nanoemulzije, ciljano oslobađanje lijekova

NANOEMULSIONS AS SYSTEMS FOR TARGETED DRUG DELIVERY

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INTRODUCTION AND OBJECTIVE

Nanoemulsions are thermodynamically stable, isotropic dispersions of two immiscible liquids stabilized using an appropriate surfactant. Various drugs or biomulecules can be incorporated in internal dispersed phase or adsorbed on external phase of nanoemulsions. Nanoemulsions have non-toxic composition which possesses great physical and biological stability and they can be sterilized or lyophilised. Manufacturing process is relatively simple and inexpensive. Hence they offer considerable opportunities for targeted drug delivery and extensive research has been conducted on the formation, characterization, and potential applications of nanoemulsions.

METHODS

Studies dealing with this issue were examined and compared. The type of research was descriptive and retrospective. Original articles published in medical journals, as well as Medline and Google Scholar databases, were used as sources of information.

RESULTS

Nanoemulsions can be used to enhance the oral bioavailability of drugs, including proteins or peptides and hydrophobic molecules. They offer improved drug solubilization and protection against enzymatic hydrolysis, as well as the potential for enhanced absorption afforded by surfactant-induced membrane fluidity and thus permeability improvement [1].

In order to achieve optimal bioavailability and minimal skin irritancy in dermal and transdermal aplication, chemical penetration enhancers can be incorporated in nanoemulsions to fluidize the *stratum corneum* lipid bilayers, thus reducing the primary skin barrier and increasing permeation [2].

Nanoemulsion can pass reticuloendothelial system of blood-brain barrier and thus have excellent potential for drug delivery to the brain. Nanoemulsion based nasal sprays could provide a good drug delivery alternative for the treatment of brain related clinical conditions which require rapid onset of action [3].

CONCLUSIONS

Nanoemulsions have many adventages in comparison to convenctional drug forms. They have great penetration ability and thus can be used as vehicles for targeted drug delivery. They can be transported through capillaries, avoid phagocytic uptake and accomplish functions such as enhanced absorption, long circulating and targeted drug delivery. Nanoemulsions improve drug efficancy and stability thus reducing their toxic side-effects. They are also biodegradibile, and temperature and pH sensitive what can be used in controled drug release.

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[3] Shinde RL, Jindal AB, Devarajan PV. Microemulsions and nanoemulsions for targeted drug delivery to the brain. Current nanoscience. 2011;7:119-133.

KEYWORDS : nanoemulsions, targeted drug delivery

POSTER

USPOREDBA METODA LASERSKE DIFRAKCIJE I ANALIZE SLIKA OPTIČKIM MIKROSKOPOM ZA ODREĐIVANJE VELIČINE ČESTICA U POLUČVRSTIM PREPARATIMA

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UVOD I CILJ

Temeljno pitanje analize veličine čestica je dobivanje različitih rezultatata za veličinu čestica izmjerenih različitim metodama, što se u velikoj mjeri može pripisati obliku čestica i mehanizmu disperzije. Kako bi se omogućio odabir najprikladnije ili optimalne tehnike, često je potrebna unakrsna korelacija između različitih tehnika [1]. Ova studija prezentira dvije tehnike mjerenja veličine čestica u Sulfadiazin 1% kremi kao jednom od novijih zahtjeva kvaliteta u polučvrstim proizvodima.

METODE

Dvije metode mjerenja veličine čestica korištene su za Sulfadiazine 1% kremu, laserska difrakcija (LD) i analizu slike optičkom mikroskopom (IA). Razvijena je vlažna metoda LD uz korištenje vode kao disperzijski medij, a korišten je 0,9% natrijev klorid kao disperzijsko otapalo. Instrument Mastersizer 2000 koristi se s parametrom instrumentalne metode: indeks loma 1,50; Apsorpcija 0,0. Za analizu optičke mikroskopije upotrijebljen je instrumentni mikroskop Olympus BX 51 sa Sensir QualID softverom.

REZULTATI

Rezultati za obje metode u Sulfadiazin 1% kremi prikazani su u tabelama 1 i 2.

Tabela 1. *Veličina čestica laserske difrakcije*

Limit	Serija br.01	Serija br.02
D (0,9) < 10 µm	90,23%	97,05%
D (1) < 100 µm	100%	100%

Table 2. *Optička mikroskopska analiza slike veličina čestica*

Limit	Serija br.01	Serija br.02
Max. 100 µm	33,52	23,27

ZAKLJUČCI

Rezultati obje metode za kremu pokazuju slične i usklađene rezultate gdje je veličina većine čestica oko 10 µm. Čestice su daleko ispod regulatrono preporučene veličine, gdje je granica definirana kao maksimalno 100 µm za kremu. S obzirom na to da LD metoda može pokazati različite rezultate uz promjenu parametara instrumentalne metode, potrebno je potvrditi veličinu čestica jednostavnijom metodom, poput manualne ili automatizirane analize optičke mikroskopije. Veličina čestica mora biti usklađena između dvije metode da bi se rezultat smatrao prihvatljivim.

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KLJUČNE RIJEČI: sulfadiazin, krema , veličina čestica, laserska difrakcija, analizu slike optičkom mikroskopom

PARTICLE SIZE DETERMINATION IN SEMISOLID FORMULATIONS WITH COMPARISON OF LASER DIFFRACTION METHOD AND OPTICAL MICROSCOPY IMAGE ANALYSIS METHOD

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INTRODUCTION AND OBJECTIVE

The fundamental issue with particle size analysis is the variety of equivalent particle diameters generated by different methods, which is largely ascribable to the particle shape and particle dispersion mechanism involved. Thus, to enable selection of the most appropriate or optimal sizing technique, cross-correlation between different techniques may be required [1]. This study present two technique for particle size measurment in Sulfadiazine 1% cream, as one of the more recent quality requirements in semi-solid products.

METHODS

Two analitical methods of particle size were developed for Sulfadiazine 1% cream, laser diffraction (LD) and optical microscopy image analysis (IA). Wet method LD is developed where water is dispersion medium and 0,9% sodium chloride was used as dispersion solvent. Mastersizer 2000 instrument is used with instrumental method parameter: refractive index 1,50; Absorption 0,0;

Optical microscopy image analysis method used instrument microscope Olympus BX 51 with Sensir QualID softwer.

RESULTS

Results for both methods in Sulfadiazine 1% cream were presented in Table 1 and 2.

Table 1. *Laser diffraction particle size*

Limit	Batch No.01	Batch No.02
D (0,9) < 10 µm	90,23%	97,05%
D (1) < 100 µm	100%	100%

Table 2. *Optical microscopy image analysis particle size*

Limit	Batch No.01	Batch No.02
Max. 100 µm	33,52	23,27

CONCLUSIONS

Results for both methods for cream show similar and harmonized results where the largest amount of particles are near 10 µm. Particles size are below regultory recommended size where limit is defined as maximum 100 µm for cream. Regarding the fact that LD method could give differrent result with change in parameter of instrument method it is neccesary to confirm particle size with simplified method like manualy or automatised optical microscopy image analysis. Particle size have to be harmonised between two method to confirm result.

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KEY WORDS Sulfadiazine, cream, particle size, laser diffraction, optical microscopy image analysis

POSTER

FORMULACIONA I FUNKCIONALNA ISPITIVANJA OKULARNIH LUBRIKANASA KOJI SADRŽE NATRIJUM-HIJALURONAT I HIDROKSIPROPIL GUAR GUMU

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UVOD I CILJ

Mukoadhezivni polimeri ulaze u sastav okularnih lubrikanasa za tretiranje sindroma suvog oka. Kada odgovarajući okularni lubrikans dođe u kontakt sa epitelom rožnjače, zabilježena interakcija između polimera iz lubrikansa i mucina [1]. Cilj ove studije bila je procjena fizičkohemijskih i funkcionalnih karakteristika izrađenih okularnih lubrikanasa koji sadrže natrijum-hijaluronat (NH) i hidroksipropil guar gumu (HPGG) pojedinačno ili u kombinaciji.

METODE

Izrađeni su okularni lubrikanski koji sadrže NH (0,4% m/V)(F1), HPGG (0,25% m/V)(F2) i njihova kombinacija (F3), uz dodatak pomoćnih supstanci, sterilisani i čuvani u periodu od mjesec dana. Kod izrađenih formulacijama sprovedeno je ispitivanje bistrine, pH, osmolalnosti, reoloških i mukoadhezivnih karakteristika uz poređenje sa komercijalno dostupnim kapima za oči Proculin Tears® (PT) (Alkaloid AD, Sjeverna Makedonija) koje sadrže NH i Systane® Ultra Lubricant (SU) (Alcon Laboratories, Inc., USA) koje sadrže HPGG. Viskozitet je mjeren primjenom rotacionog reometra na 20°C i 34°C (nakon dodavanja vještačke suzne tečnosti-VST). Mukoadhezivnost je procijenjena na osnovu rotacionih i viskoelastičnih mjerenja.

REZULTATI

pH vrijednost, osmolalnost i bistrina bili su u prihvatljivom opsegu za oftalmološke preparate. Zabilježen je značajno viši viskozitet formulacije F3 (73,1 mPa·s) u poređenju sa F1 (3,7 mPa·s) i F2 (7,4 mPa·s). Razblaživanje sa VST uzrokovalo je dvostruko povećanje viskoziteta kod F2 i SU, značajno smanjenje kod F3 dok kod F1 i PT nije bilo značajnih promjena. Nakon autoklaviranja i čuvanja, formulacija F1 je pokazala neznatne promjene fizičkohemijskih karakteristika i najvišu vrijednost mukoadhezivnog indeksa (74,9). Dodatno, vrijednosti viskoelastičnih parametara sa promjenom frekvencije ($G' \leq G''$) ukazali su na fizičko preplitanje polimera i mucina, slično prethodno dobijenim rezultatima sa lubrikansima na bazi polisaharida [2].

ZAKLJUČCI

Uzimajući u obzir jednostavnost izrade, optimalne fizičkohemijske i funkcionalne karakteristike za oftalmološke preparate i kratkoročnu stabilnost, lubrikansi koji sadrže NH i HPGG, kao i njihovu kombinaciju u odgovarajućim koncentracijama mogu se koristiti za *ex tempore* izradu oftalmoloških preparata.

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KLJUČNE RIJEČI: okularni lubricansi, mukoadhezivni polimeri, natrijum-hijaluronat, hidroksipropil guar guma

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FORMULATION AND FUNCTIONALITY ASSESSMENT OF OCULAR LUBRICANTS CONTAINING SODIUM HYALURONATE AND HYDROXYPROPYL GUAR GUM

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INTRODUCTION AND OBJECTIVE

Mucoadhesive polymers are used in ocular lubricants for the management of dry eye syndrome. Polymer-mucin force of interaction has been reported when appropriate polymers from the lubricant interact with corneal epithelium [1]. The aim of this study was evaluation of physicochemical and functional properties of compounded ocular lubricants containing sodium hyaluronate (SH) and hydroxypropyl guar gum (HPGG) alone or in combination.

METHODS

The ocular lubricants containing SH (0.4% m/V) (F1), HPGG (0.25% m/V) (F2) and their combination (F3) were compounded, with addition of auxiliary substances, sterilized and stored for one-month. The formulations were evaluated for clarity, pH, osmolality, rheological and mucoadhesive properties and compared with SH-containing Proculin Tears® (PT) (Alkaloid AD, North Macedonia) and HPGG-containing Systane® Ultra Lubricant (SU)(Alcon Laboratories, Inc., USA) commercial eye drops. The viscosity was measured using a rotational rheometer at 20°C and 34°C (after addition of the simulated tear fluid-STF). Mucoadhesion was estimated by rotational and viscoelastic rheological measurements.

RESULTS

The pH, osmolality and clarity were within the acceptable range for ophthalmic preparations. Significantly higher viscosity of formulation F3 (73.1 mPa·s) compared to F1 (3.7 mPa·s) and F2 (7.4 mPa·s) was observed. The dilution with STF induced ~2-fold viscosity increase for F2 and SU, significant decrease for F3 and no significant change in viscosity for F1 and PT. After autoclaving and storage, F1 showed negligible alterations of the physicochemical properties and the highest value of mucoadhesion index (74.9). Additionally, frequency sweep measurements indicated on physical entanglements between polymer and mucin ($G' \leq G''$), similar to previous findings with polysaccharide-based lubricants [2].

CONCLUSIONS

Considering simplicity of preparation, optimal physicochemical and functional properties for ophthalmic preparations and short-term stability, lubricants with SH and HPGG, and their combination in adequate concentrations could be used for extemporaneously compounded ocular preparations.

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KEYWORDS: Ocular lubricants, Mucoadhesive polymers, Sodium hyaluronate, Hydroxypropyl guar gum

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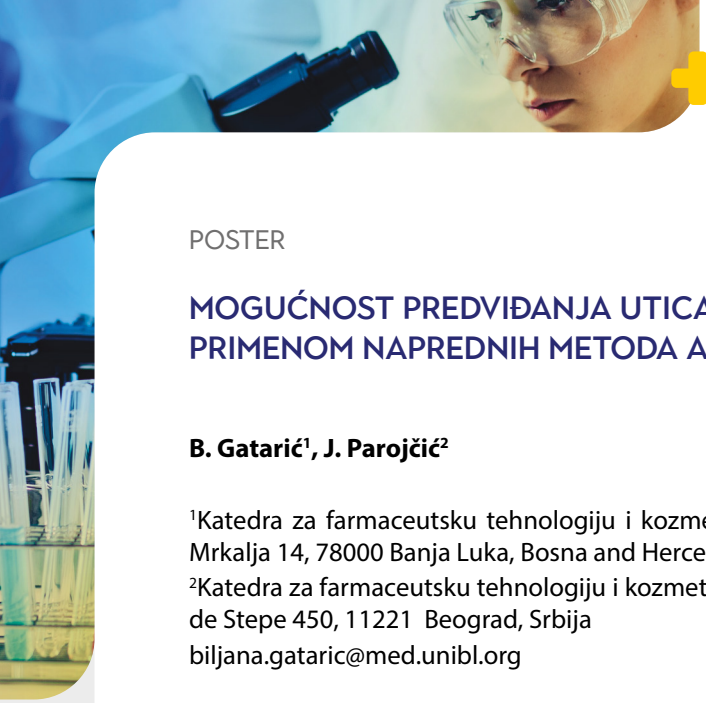

POSTER

MOGUĆNOST PREDVIĐANJA UTICAJA HRANE NA OBIM APSORPCIJE LIJEKOVA PRIMENOM NAPREDNIH METODA ANALIZE PODATAKA

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UVOD I CILJ

Uticaj hrane je prepoznat kao jedan od glavnih izazova za apsorpciju oralno primijenjenog lijeka (1). U ovoj studiji su primenom naprednih metoda analize podataka (engl. *data mining*) razvijena dva klasifikaciona modela za predviđanje uticaja hrane na obim apsorpcije lijeka.

METODE

Klinički podaci o uticaju hrane za 53 odabrana lijeka su prikupljeni iz literatura. Uticaj hrane je definisan kao "pozitivan", "negativan" ili "bez efekta" i označen kao F↑, F↓ i F0, redom.

Klasifikacioni modeli su konstruisani pomoću stabla odluke (engl. *Random forest* (RF)) i metode potpornih vektora sa polinomijalnom kernel funkcijom (engl. *Support Vector Machine with polynomial kernel function* (SVMPoly)) na osnovu odnosa doza/rastvorljivost (D/S), efektivne permeabilnosti (P_{eff}), metabolisanog procenta doze (Fm) i poluvremena eliminacije ($\tau_{1/2}$) kao ispitivanih varijabli. Klasifikacioni modeli su evaluirani pomoću vrijednosti preklapanja (engl. *recall*), preciznosti klasifikacije (engl. *precision*) i kappa vrijednosti koji su dobijeni za test set sa 15 lijekova.

REZULTATI

Kappa vrijednosti za oba modela su bile iznad željene vrijednosti od 0.4 (2,3). Vrijednosti preklapnja za oba modela su bile 0.9 u F0, 1 u F↑ i 0.67 u F↓ klasi. Dok je preciznost u F↓ klasi bila 1 za oba modela, preciznost u F0 klasi je bila veća kod SVMPoly modela (0.67) u odnosu na RF model (0.5).

Dobijeni rezultati upućuju na to da se uticaj hrane ne očekuje u slučaju lijekova koji se obimno metabolišu, imaju nizak D/S odnos, kratko poluvrijeme eliminacije i visoku permeabilnost. Lijekovi sa niskim D/S odnosom, koji se slabo metabolišu i imaju nisku permeabilnost i kratko poluvrijeme eliminacije su klasifikovani u F↓ klasu. Lijekovi iz F↑ klase su imali nizak D/S odnos, visoku permeabilnost i metabolizam.

ZAKLJUČCI

Konstruisani modeli predstavljaju obećavajuće alatke za predviđanje uticaja hrane. Mogu se koristiti za predviđanje uticaja hrane u ranoj fazi kliničkog razvoja lijeka.

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KLJUČNE RIJEČI: apsorpcija, uticaj hrane, klasifikacija.

AN INVESTIGATION INTO APPLICABILITY OF DATA MINING METHODOLOGY FOR FOOD EFFECT PREDICTION

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INTRODUCTION AND OBJECTIVE

Food effect has been recognized as one of the main challenges in oral drug absorption (1). In the present study two classification models were constructed to predict the food effect on the extent of drug absorption.

METHODS

Clinical data on the food effect for 53 selected drugs were collected from the literature. Food effect was defined as "positive", "negative" or "no effect" and designated as F↑, F↓ and F0, respectively.

The classification models were constructed using Random Forest (RF) and Support Vector Machine with polynomial kernel function (SVMPoly) methods (RStudio V1.2.1335) based on drug dose/solubility ratio (D/S), effective permeability (P_{eff}), the percent of dose metabolized (Fm) and elimination half-life ($\tau_{1/2}$) as investigated variables. Recall, precision and kappa values were used to evaluate the classification models on the test set containing 15 drugs.

RESULTS

Kappa values for both models were above the desired level of 0.4 (2,3). The recall values for both models were 0.9, 1 and 0.67 in the F0, F↑ and F↓ class, respectively. Whereas precision for the F↓ class was 1 for both models, the precision in the F0 class for SVMPoly model was higher than that of RF model (1 versus 0.9). RF model produced higher precision compared to SVMPoly model in the F↑ class (0.67 versus 0.5).

The results obtained indicate that food effect is not expected in the case of extensively metabolized drugs with low D/S, short $\tau_{1/2}$ and high permeability. Drugs with low D/S, which are poorly metabolized and have low permeability and short $\tau_{1/2}$ are classified in F↓ class by both models, while drugs from the F↑ class were characterized with high D/S, high permeability and metabolism.

CONCLUSIONS

Constructed models are promising tools for the prediction of food effect. They may be used to predict the possible food effect in early clinical development.

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KEY WORDS: drug absorption; food effect; classification.

POSTER

MIKROBIOLOŠKI KVALITET KOZMETIČKIH PROIZVODA ISPITANIH U IZJZ REPUBLIKE SRPSKE

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UVOD I CILJ

Kozmetički proizvodi, u okviru kojih spadaju sredstva za održavanje lične higijene, njegu i uljepšavanje lica i tijela, kao i dekorativna šminka ispituju se na zdravstvenu ispravnost u Institutu za javno zdravstvo Republike Srpske. Cilj rada je sagledavanje mikrobiološke ispravnosti kozmetičkih proizvoda i dekorativne šminke.

METODE

U radu su prikazani rezultati analiza uzoraka na mikrobiološku ispravnost kozmetičkih proizvoda u toku 2017. godine. Podaci o mikrobiološkoj ispravnosti su preuzeti iz godišnjeg izvještaja o zdravstvenom stanju stanovništva Republike Srpske koji izrađuje Institut za javno zdravstvo Republike Srpske[1].

REZULTATI

Za period januar-decembar 2017. godine na mikrobiološku ispravnost je analizirano oko 292 uzoraka. Mikrobiološka ispitivanja podrazumijevala su ispitivanja na sledeće mikroorganizme: kolgulaza pozitivne stafilokoke, proteus vrstu, *E. coli*, *P. aeruginosa*, ukupni broj mezofilnih aerobnih bakterija, ukupni broj kvasaca i spora plesni. Od ukupnog broja mikrobiološki kontrolisanih kozmetičkih proizvoda 32,8% uzoraka potiče iz uvoza i 67,2% iz proizvodnje. Rezultati laboratorijske kontrole pokazuju da je zabilježena mikrobiološka neispravnost 2,7% uzoraka.

ZAKLJUČCI

Među ispitanim uzorcima je mali broj neispravnih rezulatata, što predstavlja stastistički zanemarljivu neispravnost. Može se zaključiti da je zdravstvena ispravnost kozmetičkih preparata zadovoljavajuća i na visokom nivou.

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KLJUČNE RIJEČI: kozmetički proizvodi, dekorativna šminka, domaći proizvodi, zdravstvena ispravnost, IZJZ

MICROBIOLOGICAL QUALITY COSMETIC PRODUCTS SAFETY TESTING IN PUBLIC HEALTH INSTITUTE OF THE REPUBLIC OF SRPSKA

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INTRODUCTION AND OBJECTIVE

The everyday usage products, among those cosmetic products, decorative make up, personal hygiene products and cosmetic products for face and body care safety are tested daily in an laboratory of Public Health Institute of the Republic of Srpska. The aim of this paper was assessment of cosmetic products and products of decorative make up safety.

METHODS

Cosmetic products samples were analyzed by standard methods, and database was formed according to results. This database is updated annually. The results of microbiological testing during the period januar-december 2017 year are showed [1].

RESULTS

During the period januar-december 2017, 292 microbiological samples were tested per year. Microbiological tests include: Proteus, *E. coli*, coagulase + staphilococae, *P. aeruginosa*, mesophilic aerobic bacteria, fungal spores and yeasts. Of the total number of consumer goods inspected for microbiological safety, 32.8% samples come from imports and 67.2% from production. Results of laboratory inspection of consumer goods show that of the total number of samples inspected for microbiologically safety 2.7% samples were non-compliant.

CONCLUSIONS

There were a little number unsatisfactory results and it was non-statistically significant. We concluded that cosmetic products safety is satisfactory and it is on hight level.

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KEY WORDS: cosmetic products, products of decorative make up, products safety, Public Health Institute

POSTER

PROCJENA BRZINE RASTVARANJA IBUPROFENA IZ ČVRSTIH FARMACEUTSKIH OBLIKA: UPOREDNA ISPITIVANJA PREPARATA DOSTUPNIH NA TRŽIŠTU BOSNE I HERCEGOVINE

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UVOD I CILJ

Ibuprofen je široko korišćeni analgetik, antipiretik i antiinflamatorni lijek iz grupe nesteroidnih antiinflamatornih lijekova (NSAIL). Budući da ibuprofen pripada II grupi Biofarmaceutskog sistema klasifikacije (BSK), njegova niska rastvorljivosti može uticati na biološku raspoloživost nakon oralne primjene [1]. *In vitro* ispitivanje brzine rastvaranja ljekovite supstance iz farmaceutskih oblika se široko koristi pri razvoju i registraciji generičkih lijekova, kontroli kvaliteta, te predviđanju *in vivo* ponašanja određenih proizvoda [2]. Cilj ove studije bila je procjena karakteristika brzine rastvaranja ibuprofena (400 mg) iz preparata (A-G tablete; H meke kapsule) dostupnih na tržištu Bosne i Hercegovine.

METODE

Ispitivanje brzine rastvaranja sprovedeno je pod eksperimentalnim uslovima opisanim u USP42–NF 37 [3]. Uzorci su analizirani spektrofotometrijski na 264 nm. Izračunata je količina rastvorenog lijeka i rezutati su analizirani statistički. Poređenje dobijenih profila brzine rastvaranja lijeka iz različitih proizvoda sprovedeno je primjenom model-nezavisnog i model-zavisnog pristupa.

REZULTATI

Najveća količina rastvorenog lijeka zabilježena je kod proizvoda H, ali dobijeni porast nije bio značajno veći u odnosu na kumulativnu količinu ibuprofena raastvorenog iz proizvoda C i F. Brzina rastvaranja lijeka je bila jnajveća iz proizvoda B, E i F pri čemu je iz svakog proizvoda rastvoreno više od 85% od deklarisane količine lijeka unutar prvih 10 minuta. Profil brzine rastvaranja ibuprofena iz proizvoda B bio je sličan profilima dobijenim za proizvode D, E i F, što je potvrđeno i vrijednostima faktora sličnosti. Takođe, sličnost u profilima brzine rastvaranja potvrđena je i kod A-D, C-G, D-G i E-F parova. Brzina rastvaranja lijeka iz većine ispitivanih proizvoda odgovarala je Weibull kinetičkom modelu.

ZAKLJUČCI

Kako su u profilima brzine rastvaranja ibuprofena 400 mg iz različitih proizvoda dostupnih na tržištu Bosne i Hercegovine pronađene varijacije, njihova međusobna zamjena treba da bude potkrijepljena *in vivo* studijama bioekivalencije.

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KLJUČNE RIJEČI: ibuprofen, *dissolution* test, *in vitro* brzina rastvaranja lijeka, tablete, kapsule

Zahvalnica: *Autori se zahvaljuju Ministarstvu za naučnotehnološki razvoj, visoko obrzovanje i informacione tehnologije Republike Srpske (projekat 19/6-020/961-73/18) i Medicinskom fakultetu, Univerziteta u Banjoj Luci na finansijskoj podrški.*

ASSESSMENT OF DISSOLUTION PROPERTIES OF IBUPROFEN SOLID DOSAGE FORMS: COMPARATIVE EVALUATION OF PRODUCTS COMMERCIALLY AVAILABLE IN BOSNIA AND HERZEGOVINA

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INTRODUCTION AND OBJECTIVE

Ibuprofen is a widely used analgesic, antipyretic and anti-inflammatory drug from the non-steroidal anti-inflammatory drugs (NSAID) group. Given that ibuprofen is a BCS (*Biopharmaceutical Classification System)* class II drug, its low solubility can affect the bioavailability after oral use [1]. *In vitro* dissolution testing is an important tool widely employed in development and approval of generic dosage forms, quality control and prediction of the *in vivo* performance of certain products [2]. The aim of this study was the assessment of dissolution properties of drug products containing ibuprofen (400 mg) (A-G tablets; H soft capsules) commercially available in Bosnia and Herzegovina.

METHODS

Dissolution test was conducted utilizing experimental conditions proposed in USP42-NF37 [3]. The withdrawn samples were analyzed spectroscopically at 264 nm. The amount of drug dissolved was calculated and statistically analyzed. Comparison of the dissolution profiles obtained with different products was performed using model-independent and model-dependent approaches.

RESULTS

The highest drug amount was dissolved from product H, but the obtained increment was insignificant in comparison with the results obtained with C and F products. B, E and F products provided the shortest dissolution time with the fastest pattern of drug release, in which each product released more than 85% of the labeled drug within 10 minutes. Dissolution profile of B product was similar to the profiles of D, E and F, confirmed by the calculated values of similarity factors. Also, a similarity of the dissolution profiles was found between A-D, C-G, D-G and E-F pairs. Drug release from the majority of the investigated products fitted best to the Weibull kinetic model.

CONCLUSIONS

The variations in the dissolution profiles of ibuprofen (400 mg) products commercially available in Bosnia and Herzegovina were found, suggesting that interchangeability between them must be demonstrated with *in vivo* bioequivalence studies.

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KEYWORDS: ibuprofen, dissolution test, *in vitro* drug dissolution, tablets, capsules

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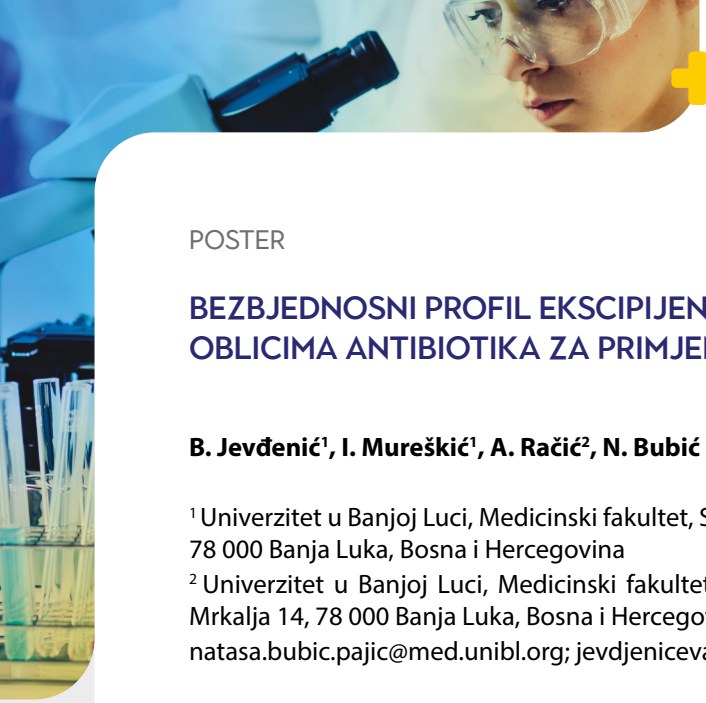

POSTER

BEZBJEDNOSNI PROFIL EKSCIPIJENASA KORIŠĆENIH U ORALNIM FARMACEUTSKIM OBLICIMA ANTIBIOTIKA ZA PRIMJENU U PEDIJATRIJI

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UVOD I CILJ

Antibiotici, kao najčešće propisivani lijekovi za djecu, često se koriste ambulantno u pedijatrijskoj praksi za liječenje akutnih respiratornih infekcija na koži/mukozi, te urinarnih infekcija [1]. Pored dobro poznatih neželjenih dejstava izazvanih aktivnim farmaceutskim supstancama, kao što su alergijske reakcije, gastrointestinalne smetnje, razvoj antimikrobne rezistencije, potencijalno štetni efekti mogu poticati i od ekscipijenasa. Različiti farmaceutski oblici antibiotika namijenjeni za oralnu primjenu kod djece su dospuni na tržištu Bosne i Hercegovine: oralne suspenzije, sirupi i praškovi za oralne suspenzije. Cilj ove studije bio je identifikovati i analizirati bezbjednosne profile ekscipijenasa prisutnih u registrovanim oralnim preparatima antibiotika za primjenu kod djece.

METODE

U cilju dobijanja informacija o kvalitativnom i kvantitativnom sastavu analiziranih preparata (n = 32), sažeci karakteristika lijeka za svaki su preuzeti sa internet stranice Agencije za lijekove i medicinska sredstva Bosne i Hercegovine.

REZULTATI

Zaslađivači su bili prisutni u svim analiziranim preparatima, od čega devet sadrže dva, a četiri preparata sadrže tri različita zaslađivača. Saharoza je bila sastojak navećeg broja analiziranih lijekova (53,1%) te bi primjenu ovih preparata trebalo izbjegavati kod pedijatrijskih pacijenata sa intolerancijom na fruktozu i pacijenata sa diabetesom [2]. Takođe, hronična upotreba saharoze može prouzrokovati karijes zuba [2]. Vještački zaslađivači (saharin, aspartam, ciklamat) povezani sa mogućim kancerogenim efektima, korišćeni su u 65,6% testiranih uzoraka. Ispitivani preparati (31,3%) su bili konzervisani benzoatima za koje je poznato da izazivaju nenatalnu žuticu. Preostalih 18,7% konzervisano je parabenima koji mogu izazvati preosjetljivost, simptome astme i hiperbilirubinemiju kod novorođenčadi [3]. Arome i boje, sastojci 96,9% odnosno 34,4% preparata, potrebno je izbjegavati zbog alergijskog potencijala.

ZAKLJUČCI

Prilikom izbora odgovarajućeg lijeka neophodno je razmotriti zdravstveno stanje pedijatrijskog pacijenta i sastav preparata naročito u pogledu bezbjednosnog profila njegovih sastojaka.

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KLJUČNE RIJEČI: antibiotici, ekscipijensi, pedijatrijski, zaslađivači, konzervansi

Zahvalnica: *Autori se zahvaljuju Ministarstvu za naučnotehnološki razvoj, visoko obrzovanje i informacione tehnologije Republike Srpske (projekat 19/6-020/961-73/18) i Medicinskom fakultetu, Univerziteta u Banjoj Luci na finansijskoj podršci.*

SAFETY ASPECTS OF EXCIPIENTS USED IN PEDIATRIC ORAL DOSAGE FORMS CONTAINING ANTIBIOTICS

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INTRODUCTION AND OBJECTIVE

Antibiotics, common prescription drugs for children, are mainly used in the ambulatory pediatrics practice to treat respiratory, skin/mucosal or urinary infections [1]. Beside their known side effects induced by the active pharmaceutical ingredients, such as allergic reactions, gastrointestinal disorders and antimicrobial resistance development, potential adverse effects can also derive from excipients. Different dosage forms of antibiotics intended for oral use in children are commercially available in Bosnia and Herzegovina: oral suspensions, syrups and powders for oral suspensions. The aim of this study was to identify and analyze safety profiles of excipients in authorized oral antibiotics preparations for pediatric use.

METHODS

In order to obtain the information on qualitative and quantitative composition of the investigated preparations (n = 32), summary of product characteristics for each product was downloaded from the web site of Agency for medicinal products and medical devices of Bosnia and Herzegovina.

RESULTS

Sweeteners were present in all investigated products, with nine and four products containing two and three different sweeteners, respectively. Since sucrose was the constituents of the majority of analyzed drug products (53.1%), their use in pediatric patients suffering from fructose intolerance and diabetic patients should be avoided [2]. Also, chronic use of sucrose may promote dental caries [2]. Artificial sweetens (saccharine, aspartame, cyclamate), associated with possible cancer-inducing effects, were used in 65.6% of the tested samples. The tested products were preserved with benzoates (31.3%), which can induce neonatal jaundice, or parabens (18.7%), causing hypersensitivity, asthma symptoms and hyperbilirubinaemia in neonates [3]. Aromas and colors added in 96.9% and 34.4% of preparations should be avoided due to their allergic potential.

CONCLUSIONS

During the selection of the most appropriate drug product, health condition of a pediatric patient coupled with product composition regarding safety profile of its constituents, should be necessarily taken into consideration.

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KEYWORDS: antibiotics, excipients, pediatric, sweeteners, preservatives.

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POSTER

REOLOŠKA MJERENJA NA LIZOZIM KREMI U TOKU ŽIVOTNOG CIKLUSA PROIZVODA

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UVOD I CILJ

Izbor i odabir lijekova koji će se koristiti u praksi može da zavisi od reoloških karakteristika proizvoda. Reološka ispitivanja polučvrstih farmaceutskih proizvoda pruža neophodne informacije koje su potrebne za procjenu osobina tih preparata, kao što su viskoznost, elastičnost, kvalitet i stabilnost čuvanja. Ispitivanja u ovom radu fokusirana su na reološke tehnike za karakterizaciju svojstava polučvrstog novog proizvoda.

METODE

Za karakterizaciju polučvrstih oblika doziranja korišteni su različiti testovi, uključujući ispitivanje testova smicanja kroz krive protoka i viskoznosti, zatim mjerenja tačke napona popuštanja te oscilatorni testovi poput skala amplitude i frekvencije. Odnos između stresa, napona i viskoelastičnog ponašanja prikazan je kroz krive na grafikonaima zvane reogrami. Tipične krive protoka prikazane su kroz korelacije $\tau = f(\gamma)$, viskoznost se prikazuje kao funkcija napona smicanja $\eta = f(\tau)$ i viskoelastičnog ponašanja u funkciji G′, G″, $G^* = f(f, \tan \delta)$. Korišteni instrument je RheoStress RS1. Instrumentalni parametri: CR=10,00 1/s; t=300 s; T=23,0 °C; Gap=0,999-1,001 mm.

REZULTATI

Ispitivano je kako vrijeme čuvanje utiče na reološke karakteristike kreme: viskoznost, napon popuštanja i viskoelastično ponašanje. Uzorci su analizirani u različitim periodima i to nakon 3, 6, 12 i 24 mjeseca od proizvodnje.

Table 1. *Rezultati za prividni viskozitet kreme u različitim periodima stajanja*

3 mjesec	6 mjesec	12 mjesec	24 mjesec
13,26	11,89	15,69	14,20

Table 2. *Rezultati za napon popuštanja*

1 mjesec		24 mjesec	
τ	|G*| in Pa	τ	|G*| in Pa
262,1	254,8	262,9	254,4

ZAKLJUČCI

Ispitivanje urađeno na lizozim kremi u periodima 3, 6, 12 i 24 mjeseca od njene proizvodnje za parametar viskoziteta pokazije da nema značajne promjene u viskoznosti tokom stajanja.

Mjerenje napona popuštanja i drugih reološki parametara takođe potvrđuje da krema ima konstantnu strukturu tokom stajanja u predviđenom periodu.

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KLJUČNE RIJEČI: reologija, viskoznost, napon popuštanja, prividni viskozitet, polučvrsti proizvody, lizozim

RHEOLOGICAL MEASUREMENTS ON LYSOZYME CREAM DURING LIFE CYCLE OF PRODUCT

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INTRODUCTION AND OBJECTIVE

The application and acceptance of pharmaceuticals which will be used in practice are also dependent on the flow properties of the final product. Rheological characterization of pharmaceutiacal semisolids is of importance as it provides fundamental information required for the assessment of some of the final properties of product such as viscosity, elasticity, quality and storage stability. This study focused on using rheological techniques to characterize the properties of new developed semisolid formulation.

METHODS

Various tests were employed to characterize the semisolid dosage forms, including continuous shear test such as flow and viscosity curve, yield point measurements and oscillatory tests. The relationship between stress, strain and viscoelastic behaviour are depicted in the so called rheograms. Typical flow curves are presented through $\tau = f(\gamma)$, viscosity is drawn as a function of the shear stress $\eta = f(\tau)$ and viscoelastic behaviour in function of G', G'', G* =f (f, tan δ). It was used RheoStress RS1 instrument. Instrument parameters were: CR=10,00 1/s; t=300 s; T=23,0 °C; Gap=0,999-1,001 mm.

RESULTS

We investigated how storage time can impact cream reology: viscosity yield point and viscoelastic behaviour . It was tested in different periods: 3, 6, 12 and 24 months after production.

Table 1. *Results for apparent viscosity in Pas*

3 month	6 month	12 month	24 month
13,26	11,89	15,69	14,20

Table 2. *Results for yiled point*

Batch No1		Batch No1	
1 month		24 month	
τ in Pa	|G*| in Pa	τ in Pa	|G*| in Pa
262,1	254,8	262,9	254,4

CONCLUSIONS

Test performed on Lysozyme cream in periods 3, 6, 12 and 24 months after its production for the viscosity parameter showed that there is no change in viscosity, yild point or other reology during stability of product.

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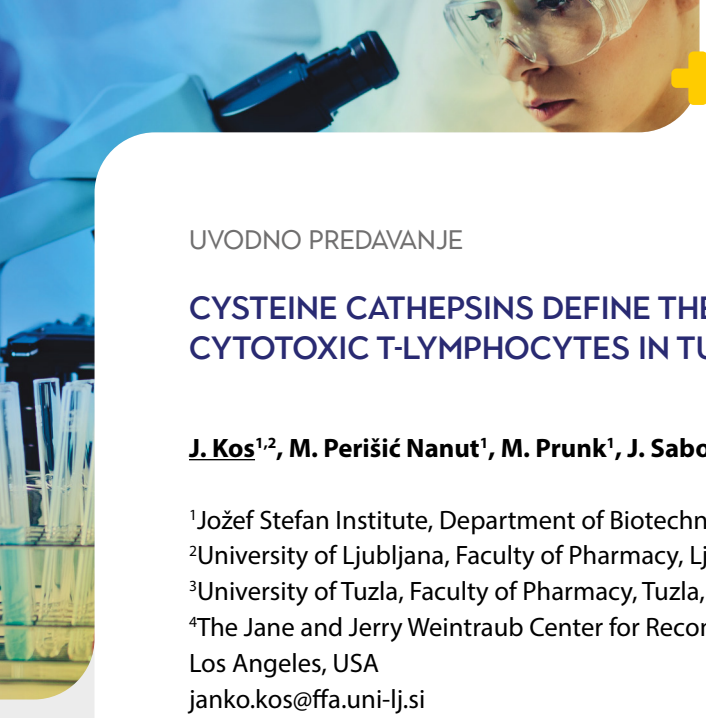
KEY WORDS: rheology, viscosity, yield strees, single point viscosity, semisolids, lysozyme

MEDICINSKA BIOHEMIJA



UVODNO PREDAVANJE

CYSTEINE CATHEPSINS DEFINE THE CYTOTOXICITY OF NK CELLS AND CYTOTOXIC T-LYMPHOCYTES IN TUMOR MICROENVIRONMENT

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INTRODUCTION: Cysteine cathepsins are involved in diverse processes of immune response, including the regulation of granule dependent cytotoxicity of cytotoxic T-lymphocytes (CTLs) and natural killer (NK) cells. The activity of cysteine cathepsins is regulated by cystatins which are in general cytosolic or extracellular proteins acting as emergency inhibitors, with exception of cystatin F which is present in endosomal/lysosomal vesicles and thus able to directly impair the activity of its targets.

AIMS: We tested whether cystatin F, derived either from immune or bystander cells in tumor microenvironment, is able to reduce NK and T cell cytotoxicity.

METHODS: Advanced methods of biochemistry, immunology, molecular and cell biology have been used in the study. In vivo, humanized-BLT mouse model have been used to test the impact of cystatin F on NK cell cytotoxicity. Two primary cell lines isolated from patients with oral cavity cancer, being stem-like/undifferentiated or differentiated, have been used to test the NK and CTL cell cytotoxicity.

RESULTS: Cystatin F expression is controlled by C/EBP α transcription factor. It is delivered to endosomal/lysosomal pathway as an inactive, disulphide-linked dimer which is transformed to a monomer after proteolytic cleavage of 15 N-terminal amino acids and truncated monomeric form becomes a potent inhibitor of cathepsins C, H and L, peptidases involved in the activation of granzymes and perforin. The glycosylation pattern and the activation of M6PR pathway are important in controlling secretion of cystatin F from target cells, as well as internalization by cytotoxic cells and trafficking to endosomal/lysosomal vesicles. In tumor microenvironment, inactive dimeric cystatin F can be secreted from cancer stem cells, less differentiated cancer cells and in particular, from monocytes and is taken up by cytotoxic cells. Subsequent monomerization and inhibition of cysteine cathepsins within the endosomal/lysosomal vesicles impair granzyme and perforin activation, and induce cell anergy. Anergic NK cells, on the other hand, by increasing cytokine secretion direct cancer stem cells and monocytes towards differentiated cells which are low in expression and secretion of cystatin F.

CONCLUSIONS: Cystatin F is therefore a mediator of the interplay between cancer stem cells, differentiated cancer cells and immune cells in tumor microenvironment.

KEY WORDS: cathepsins, cystatin F, NK cells, T lymphocytes, cancer

CISTEINSKI KATEPSINI DEFINIRAJU CITOTOKSIČNOST NK ĆELIJA I CITOTOKSIČNOST T-LIMFOCITA U TUMORSKOM MIKROOKOLIŠU

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UVOD
Cisteinski katepsini uključeni su u različite procese imunološkog odgovora, uključujući regulaciju citotoksičnosti granulata citotoksičnih T-limfocita (CTLs) i ćelija prirodnih ubica (NK). Aktivnost cisteinskih katepsina reguliraju cistatini koji su općenito citosolni ili vanćelijski proteini koji djeluju kao inhibitori u hitnim slučajevima, s izuzetkom cistatina F koji je prisutan u endosomskim / lizosomskim vezikulama i na taj način može direktno narušiti aktivnost svojih meta.

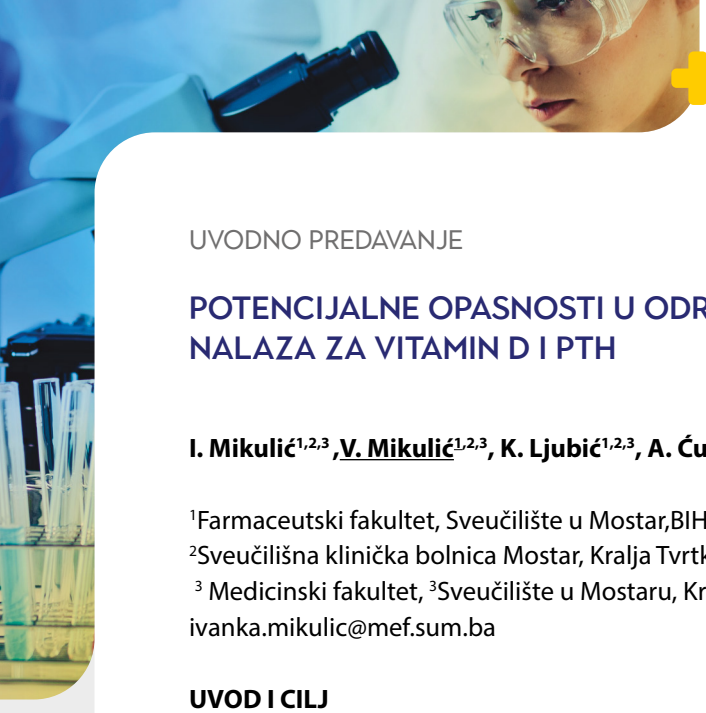
CILJEVI
Ispitali smo može li cistatin F, dobijen iz imunih ili *bystander* ćelija u tumorskom mikrookolišu smanjiti citotoksičnost NK i T stanica.

METODE
U istraživanju su korištene napredne metode biohemije, imunologije, molekularne i ćelijske biologije. *In vivo*, humanizirani-BLT model miša korišten je za ispitivanje utjecaja cistatina F na citotoksičnost NK ćelija. Za ispitivanje citotoksičnosti NK i CTL ćelija korištene su dvije primarne ćelijske linije izolirane od pacijenata s karcinomom usne šupljine, koji su slične matičnim ćelijama/nediferencirane ili diferencirane.

REZULTATI: Ekspresija cistatina F kontrolira C/EBP α faktor transkripcije. Dostavlja se endosomskom/lizosomalnom putu kao neaktivan, disulfidno povezan dimer koji se transformira u monomer nakon proteolitičkog cijepanja 15 N-terminalnih aminokiselina, a skraćeni monomerni oblik postaje moćan inhibitor katepsina C, H i L, uključenih peptidaza u aktivaciji granzima i perforina. Obrazac glikozilacije i aktivacija M6PR puta važni su za kontrolu izlučivanja cistatina F iz ciljnih ćelija, kao i za internalizaciju citotoksičnih ćelija i promet u endosomske/lizosomske vezikule. U tumorskom mikrookolišu neaktivni dimerni cistatin F može se izlučiti iz matičnih ćelija karcinoma, manje diferenciranih stanica karcinoma, a posebno iz monocita i preuzimaju ih citotoksične ćelije. Naknadna monomerizacija i inhibicija cisteinskih katepsina unutar endosomske/lizosomske vezikule smanjuju aktivaciju granzima i perforina i induciraju ćelijsku anergiju. Anergične NK ćelije, s druge strane, povećavajući izlučivanje citokina upućuju matične ćelije raka i monocite prema diferenciranim ćelijama koje su niske u ekspresiji i izlučivanju cistatina F.

ZAKLJUČCI
Cistatin F je, dakle, posrednik uzajamne interakcije između matičnih ćelija karcinoma, diferenciranih ćelija raka i imunoloških ćelija u tumorskom mikrookolišu.

KLJUČNE RIJEČI: katepsini, cstatin F, NK ćelije, T limfociti, rak



UVODNO PREDAVANJE

POTENCIJALNE OPASNOSTI U ODREĐIVANJU KONCENTRACIJE I INTERPRETACIJI NALAZA ZA VITAMIN D I PTH

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UVOD I CILJ

Za pravilnu interpretaciju laboratorijskih nalaza potrebno je poznavati i prepoznati sve potencijalne čimbenike koji mogu utjecati na rezultat svakog laboratorijskog parametra. Cjelokupni laboratorijski rad odvija se u tri povezane faze: predanalitička, analitička, postanalitička, od kojih se samo analitička faza odvija u potpunosti u laboratoriju. Udio pogreški u cjelokupnom analitičkom procesu je veći u predanalitičkoj i postanalitičkoj fazi rada (50-70 %) u odnosu na analitičku fazu (4-13 %). Uzrok tome su još uvijek nejasno definirane i standardizirane predanalitičke i postanalitičke faze laboratorijskog rada [1].

METODE

Kroz ovo predavanje pokušati će se dati pregled nekih od interferencija u predanalitičkoj fazi laboratorijskog rada kao što su lipemija, ikterija, hemoliza ili sami antikoagulansi, budući da još uvijek ne postoje smjernice kako ih otkriti u uzorcima krvi i dokumentirati. Ovim predavanjem, također, se nastoji skrenuti pažnja na interferencije svojstvene kvantitativnim imunokemijskim analizama s naglaskom na metode za vitamin D i paratireoidni hormon (PTH).

REZULTATI

Interferencije u imunokemijskim metodama definiraju se kao učinak tvari prisutnih u analitičkom sustavu koje uzrokuju promjenu izmjerene koncentracije u odnosu na pravu koncentraciju analita. Na interferencije u imunokemijskim metodama treba pomisliti ako se dobije neprihvatljiv rezultat, ako postoji nelinearnost prilikom razrjeđivanja, ako nema podudarnosti s ostalim nalazima, odnosno kliničkim podacima, ako se različitim imunokemijskim metodama dobiju značajno različiti rezultati određivanja istog analita [2]. Pritom se naglašava opasnost od interferencija biotinom, koje mogu rezultirati lažno povećanim ili lažno smanjenim koncentracijama vitamina D i PTH, te pogrešnom interpretacijom laboratorijskih nalaza što može imati fatalne posljedice kod postavljanja dijagnoze kao što su hiper ili hipoparatireoidizam [3].

ZAKLJUČCI

Laboratorijski rad je složen proces koji ima za cilj izdavanje nalaza, koji moraju biti vjerodostojni i pravilno interpretirani. Na taj način nalaz postaje ključni dokument u donošenju medicinskih odluka. Glavni cilj ovog predavanja je pomoći liječnicima pri interpretaciji laboratorijskih nalaza s naglaskom na problematiku laboratorijske medicine u endokrinologiji.

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KLJUČNE RIJEČI: interferencije, predanalitika, biotin, vitamin D, PTH

POSSIBLE DANGERS IN DETERMINATION OF CONCENTRATION AND INTERPRETATION OF VITAMIN D AND PTH FINDINGS

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INTRODUCTION AND OBJECTIVE

For the proper interpretation of laboratory findings, it is necessary to know and identify all potential factors that may affect the result of each laboratory parameter. The whole laboratory work is carried out in three related phases: pre-analytical, analytical, post-analytical, of which only the analytical phase takes place completely in the laboratory. The proportion of errors in the overall analytical process is higher in the pre-analytical and post-analytical phase (50-70%) compared to the analytical phase (4-13%). This is due to the still vaguely defined and standardized pre-analytical and post-analytical phases of laboratory work [1].

METHODS

This lecture will attempt to give an overview of some of the interferences in the pre-analytical phase of laboratory work, such as lipemia, hyperbilirubinemia, hemolysis, or the anticoagulants themselves, since there are still no guidelines for how to detect and document them in blood samples. This lecture also seeks to draw attention to the interferences inherent in quantitative immunochemical analyzes with an emphasis on methods for vitamin D and parathyroid hormone (PTH).

RESULTS

Interferences in immunochemical methods are defined as the effect of substances present in the analytical system that cause a change in the measured concentration relative to the true concentration of the analyte. Interferences in immunochemical methods should be considered if an unacceptable result is obtained, if there is non-linearity in the dilution, if there is no agreement with other findings or clinical data, if different immunochemical methods yield significantly different results from the determination of the same analyte [2]. It emphasizes the risk of biotin interference, which can result in false-elevated or falsely reduced concentrations of Vitamin D and PTH, and misinterpretation of laboratory findings, which can have fatal consequences when diagnosed as hyper or hypoparathyroidism [3].

CONCLUSIONS

Laboratory work is a complex process that aims to reveal findings, which must be credible and properly interpreted. In this way, finding becomes a key document in medical decision making. The main objective of this session is to assist physicians in the interpretation of laboratory results with an emphasis on issues of laboratory medicine in endocrinology.

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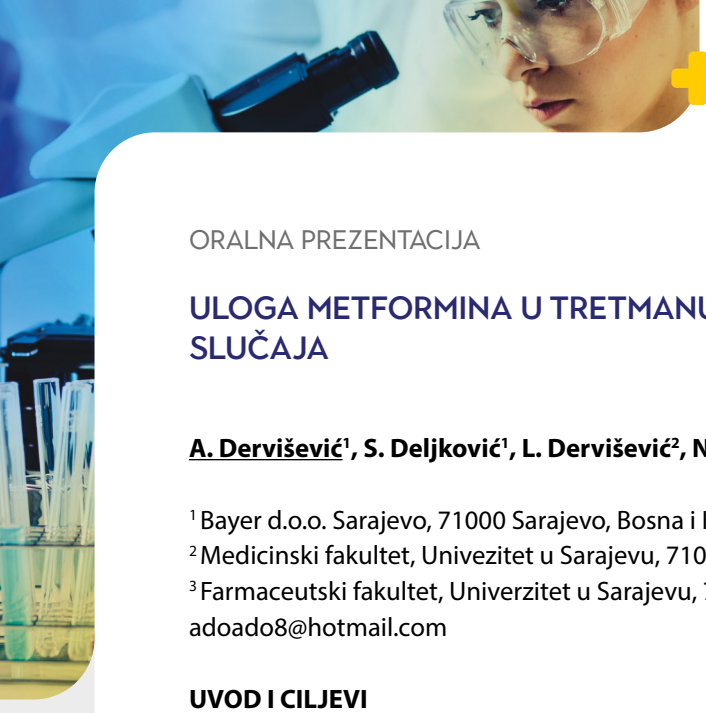
KEY WORDS: interferences, pre-analytics, biotin, vitamin D, PTH



ORALNA PREZENTACIJA

ULOGA METFORMINA U TRETMANU SINDROMA POLICISTIČNIH JAJNIKA- PRIKAZ SLUČAJA

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UVOD I CILJEVI

Sindrom policističnih jajnika (PCOS) je najčešće endokrinološko oboljenje žena koje pogađa 4 – 12% žena [1] i često je povezano sa neplodnošću zbog izostanka ovulacije [2]. Metformin je predložen u terapiji da bi se ustanovila u kojoj mjeri hiperinzulinemija utiče na patogenezu stanja.

METODE I PACIJENTI

30-godišnja pacijentica je evaluirana zbog oligomenoreje i čestih hipoglikemija. Ginekologu se obratila prvi put zbog neredovnog ciklusa i nemogućnosti začeća godinu dana. Spermiogram muža je uredan. Prethodne stimulacije ovulacije sa klomifenom, dabrostonom i humanim horionskim gonadotropinom nisu bile uspješne. Pregledom je utvrđen BMI 21, bez prekomjerne dlakavosti na bradi, podlakticama i abdomenu, bez strija, bez *acanthosis nigricans*, uredna štitna žlijezda i akne na licu. Nakon opterećenja sa 75 g glukoze, oralni test glukoze (0-30-60-90-120-180 min) pokazao je povišenu vrijednost inzulina (62-415-293-368-264-42 pmol/L. Normalne vrijednosti TSH, vitamina D, FSH, estrogena, progesterona, prolaktina, testosterona i kortizola i visoke vrijednosti LH su nađene u lutealnoj fazi. Ultrazvuk je potvrdio policistično izmijenjene jajnike. Klinički i laborarotijski nalazi su konzistentni za PCOS: Započeta je terapija sa promjenom stila života (dijeta sa niskim glikemijskim indeksom) i metforminom 500mg. Tri mjeseca od početka terapije pacijentica je zatrudnila te je rodila zdravo dijete bez komplikacija.

ZAKLJUČCI

Iako je upotreba metformina u tretmanu PCOS još nerazjašnjena, u ovom slučaju metformin je bio siguran i efikasan. Prednosti su uočene na oligomenoreju i plodnost.

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KLJUČNE RIJEČI: inzulin-osjetljivi lijekovi, metformin, sindrom policističnih jajnika (PCOS)

ROLE OF METFORMIN IN THE MANAGEMENT OF POLYCYSTIC OVARY SYNDROME RELATED INFERTILITY- CASE REPORT

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INTRODUCTION AND OBJECTIVE

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder affecting 4 – 12% of women [1], and it's often related with infertility due to lack of ovulation [2]. Metformin was intentionally introduced to establish the extent to which hyperinsulinemia influences the pathogenesis of the condition.

METHODS AND PATIENT

30-year old female patient was evaluated for oligomenorrhea, and frequent hypoglycemia. She consulted her gynecologist for the first time due to concern of irregular menstrual cycles, and inability to become pregnant for one year. Her partner's spermiogram was in order. Previous stimulation of ovulation with clomifen, dabroston and human chorionic gonadotropin were unsuccessful. Examination revealed BMI 21; no excessive hair on chin, forearms and lower abdomen; no striae, no *acanthosis nigricans*, normal thyroid, and acne skin. An oral glucose tolerance test after taking 75 g of glucose (measurements in 0-30-60-90-120-180 min) showed high levels of insulin (62-415-293-368-264-42 pmol/L). Normal level of TSH, Vitamin D, FSH, estrogen, progesterone, prolactin, testosterone and cortisol, and high LH were found in luteal phase. A pelvic ultrasound confirmed polycystic ovaries. Clinical and laboratory tests were consistent with PCOS. Therapy and treatment included lifestyle changes (low glycemic index diet) and metformin 500 mg. Three months after the treatment patient got pregnant and gave birth to a healthy baby, without any complications.

CONCLUSION

Although, the use of metformin in the treatment of PCOS is off-label, in this case, metformin had showed as safe and effective. Benefit was made on oligomenorrhea, and fertility.

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KEYWORDS: insulin-sensitizing drugs, metformin, polycystic ovary syndrome (PCOS)

ORALNA PREZENTACIJA

EFEKTI TIP 2 DIJABETESA NA ŽENE OBOLJELE OD KARCINOMA DOJKE

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UVOD I CILJ

Tip 2 dijabetes (T2D) predstavlja sve veći problem javnog zdravlja. Prema podacima iz 2017. godine, na globalnom nivou oko 425 miliona ljudi ima dijabetes. Karcinom dojke je drugi najčešći uzrok smrti kod žena i od ukupnog broja ljudi koji boluju od raznih tipova karcinoma, njih 25% boluju od karcinoma dojke. Karcinom dojke i dijabetes se često javljaju zajedno. Cilj rada je prikazati rezultate dosadašnjih istraživanja o povezanosti T2D sa karcinomom dojke i mehanizame koji stoje u podlozi ove povezanosti.

METODE

Pregled naučne i stručne literature uključujući medicinske baze podataka dostupne na internetu (*PubMed*, *Medline*, *Google Scholar*, *Springer*), knjige i naučne časopise.

REZULTATI

T2D utiče na prognozu i ishod bolesti, na način da povećava rizik od smrtnosti, povećava učestalost metastaza i rizik za recidiv karcinoma dojke. Također, ograničava terapijske mogućnosti karcinoma dojke i povećava učestalost postoperativnih komplikacija nakon mastektomije i lumpektomije. Četiri glavna mehanizma su zaslužna za povezanosti između T2D i karcinoma dojke, a to su: aktiviranje inzulinskog puta, aktivacija puta inzulinu sličnog faktora rasta (IGF-1), izmijenjena regulacija endogenih polnih hormona, te izmijenjena regulacija adipocitokina, odnosno hronična inflamacija i oksidativni stres.

ZAKLJUČCI

Studije sugerišu da T2D može biti povezan sa 10% - 20% povećanim rizikom od kancera dojke. Multifaktorijalni odnos karcinoma dojke i dijabetesa je složen i nije u potpunosti shvaćen. Razumijevanje veze između dijabetesa, oksidativnog stresa i karcinoma dojke postaje imperativ te napore treba usmjeriti na poboljšanje skrininga i razvoja mehanizama za procjenu rizika.

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[3] Chen X, Ding J, Tang J, Luo WX, Qiu M, Liu JY. The expression difference of insulin-like growth factor 1 receptor in breast cancers with or without diabetes. Journal of cancer research and therapeutics. 2015; 11(2): 295-299.

KLJUČNE RIJEČI: dijabetes, karcinom dojke

EFFECTS OF TYPE 2 DIABETES ON BREAST CANCER IN WOMAN

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INTRODUCTION AND OBJECTIVE

Type 2 diabetes T2D is a public health problem. According to estimates from 2017, 425 million people worldwide have diabetes. Breast cancer is the second most common cause of death among women and of the total number of people suffering from various types of cancer, 25% suffer from breast cancer. Breast cancer and diabetes often occur together.

The aim of this study is to present the results of previous studies on the association of T2D with breast cancer and the mechanisms of this association.

METHODS

A review of scientific and professional literature including medical databases available online (*PubMed*, *Medline*, *Google Scholar*, *Springer*), books, and scientific journals.

RESULTS

Diabetes affects the prognosis and outcome of the disease, increasing the risk of mortality, increasing the incidence of metastases and the risk of breast cancer recurrence. Diabetes limits the therapeutic capabilities of breast cancer and increases the incidence of postoperative complications after mastectomy and lumpectomy. Four major mechanisms are responsible for the connection between T2D and breast cancer, which is: activating the insulin pathway, activating pathway of insulin-like growth factor (IGF-1), modified regulation of endogenous sex hormones, and modified regulation of adipocytokine, chronic inflammation and oxidative stress.

CONCLUSIONS

Studies suggest that T2D may be associated with a 10% - 20% increased risk of breast cancer. The multifactorial relationship between breast cancer and diabetes is complex and not fully understood. Understanding the link between diabetes, oxidative stress and breast cancer is becoming imperative, and efforts should be focused on improving screening and developing risk assessment mechanisms.

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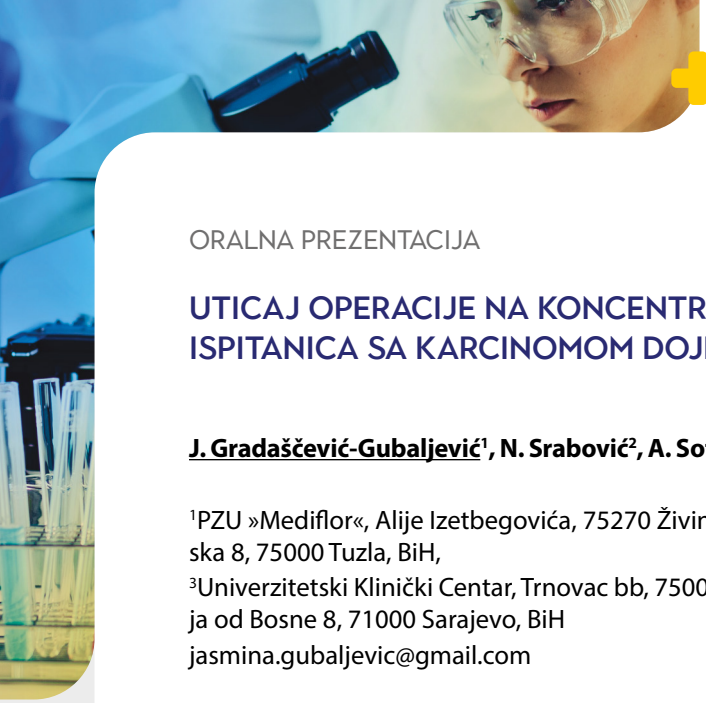
KEY WORDS: diabetes, breast cancer



ORALNA PREZENTACIJA

UTICAJ OPERACIJE NA KONCENTRACIJU MALONDIALDEHIDA U SERUMU U ISPITANICA SA KARCINOMOM DOJKE

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UVOD I CILJ

Malondialdehid kao marker oksidativnog stresa posljednjih godina je čest predmet istraživanja jer je pokazano da je njegova koncentracija povećana u serumu kod karcinoma. [1,2] U sklopu ovog istraživanja je ispitan uticaj hirurškog liječenja na nivo oksidativnog stresa.

METODE

Nivo oksidativnog stresa je ispitan određivanjem koncentracije malondialdehida u serumu, fluorimetrijski. Koncentracija malondialdehida u serumu je ispitana kod 50 pacijentica sa dijagnozom karcinoma dojke i 48 pacijentica sa dijagnozom benignog oboljenja dojke kao kontrolne grupe.

REZULTATI

U sprovedenom istraživanju nije pronađena statistički značajna razlika u koncentraciji malolndialdehida u serumu ispitanica sa malignim i benignim oboljenjem dojke prije i poslije operacije (p=0,560). Koncentracija malondialdehida je manja u serumu pacijentica nakon odstranjenja tumora. Naime, hirurški stres prvih par sati nakon operativnog odstranjenja dojke dovodi do povećanja oksidativnog stresa [3], budući da je hirurška procedura sama po sebi stres za organizam i prate je hipotermija, metabolička acidoza, koagulacija, te smanjenje antioksidativnog kapaciteta plazme. Oksidativni stres se potom smanjuje, pretpostavka je zbog odstranjenja tumora.

ZAKLJUČCI

Na osnovu sprovedenog ispitivanja značajnosti razlike u koncentraciji malondialdehida u serumu ispitanica sa malignim i benignim oboljenjem dojke, isti se ne može smatrati markerom za praćenje uticaja hirurškog stresa kod ovih populacija.

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KLJUČNE RIJEČI: karcinom dojke, malondialdehid, hirurški stres

SURGICAL STRESS INFLUENCE ON MALONDIALDEHYDE SERUM LEVELS IN BREAST CANCER PATIENTS

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INTRODUCTION AND AIM

Malondialdehyde serum levels as a marker of oxidative stress has been investigated in the resent years as it has found to be increased in diferent types of cancer.[1,2] The aim of this study was to investigate the influence of surgical stress on oxidative stress level in breast cancer.

METHODS

Oxidative stress level was examined by fluorimetrical determination of malondialdehyde serum concentration. Malondialdehyde serum levels are determined in 50 breast cancer patients and 48 patients with benign breast disease as a control group.

RESULTS

In this study, there was no significant difference between malondialdehyde serum levels in breast cancer patients and patients with benign breast disease before and after surgical tumour removal (p=0,560). Decreased malondialdehyde serum level were found after toumour removal. Particularly, surgical stress first few hours after breast cancer removal leads to increased oxidative stress [3], because surgical procedure is itself a stress for organism folowed by hypothermia, metabolic acidosis, coagulation and decreased antioxidant plasma capacity. Afterwards, the oxidative stress decreases, the assumption is bracause of tumour removal.

CONCLUSION

Based on our research on differences between serum malondialdehyde levels in patients with malign and benign breast disease, serum malondialdehyde level can not be considered as a marker of surgical stress in tested population.

LITERATURE

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[3] Basu S. et all. Eicosanoids and Adipokines in Breast cancer: From Molecular Mechanisms to Clinical Considerations, Antioxidants & redox signalling, 2013; 18(3): 323-60.

KEY WORDS: breast cancer, malondialdehyde, surgical stress

ORALNA PREZENTACIJA

PROCJENA TOKSIČNOSTI SMJESE OLOVA I KADMIJA NA HUMANIM ĆELIJSKIM LINIJAMA HL-60 I JURKAT

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UVOD I CILJ: Brojna istraživanja su pokazala da su olovo i kadmij toksični metali koji pogađaju različite ciljne molekule u ćelijama, ali malo se zna o učincima ova dva metala u smjesi, posebno na imunološke ćelije [1,2]. HL-60 ćelije i Jurkat ćelije korištene su kao modeli za ispitivanje pojedinačnog i kombinovanog citotoksičnog učinka olova i kadmija na imunološkim ćelijama. Također, analiziran je genotoksični potencijal svakog pojedinog metala.

METODE: Olovo (10-100 µM) i kadmij (2,5-10 µM) korišteni su pojedinačno i kao smjese u ćelijskim linijama tokom 24 sata inkubacije. Koncentracije Pb i Cd za analizu djelovanja smjese odabrane su iz njihovih pojedinačnih citotoksičnih učinaka. Primijenjena je metoda ispitivanja aditivnog efekta, u kojoj je koncentracija svakog spoja, ekvivalentna njegovoj IC_{20}, izračunata iz pojedinačnih krivulja citotoksičnosti [3]. Za procjenu citotoksičnosti, ćelije su inkubirane 2 sata sa Presto blue reagensom i apsorpcija je mjerena na 570 nm. Statistička analiza izvršena je Student-ovim t-testom; p vrijednosti ispod 0,05 smatrane su značajnim. Za određivanje genotoksičnosti Pb i Cd, korištena je metoda indirektne imunofluorescencije sa primarnim anti-fosfo-histonskim H2A.X antitijelom. Genotoksični učinci ispitani su hi-kvadrat testom; p vrijednosti ispod 0,05 smatrane su značajnim.

REZULTATI: Olovo i kadmij uzrokovali su citotoksične efekte u obje ćelijske linije. Kadmij je ispoljio veći citotoksični potencijal. Najizraženiji citotoksični učinak opažen je kod najnižih koncentracija metala (2,5 µM za kadmij i 25 µM za olovo). Daljnje povećanje koncentracije metala nije dovelo do proporcionalnog pada vijabilnosti ćelija u obje linije. Metalne smjese pokazale su sinergistički učinak na HL-60 ćelijama i antagonistički učinak na Jurkat ćelijama u usporedbi s pojedinačnim metalima. Kadmij je ispoljio snažniji genotoksični učinak od olova i pokazao je dozno zavisni efekat u obje ćelijske linije.

ZAKLJUČAK: Kombinovani efekti trebaju se uzeti u obzir prilikom procjene rizika od toksičnosti teških metala.

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KLJUČNE RIJEČI: smjese metala, citotoksičnost, genotoksičnost, HL-60 ćelije, Jurkat ćelije

TOXICITY ASSESSMENT OF LEAD AND CADMIUM MIXTURE ON HL-60 AND JURKAT CELL LINES

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INTRODUCTION AND OBJECTIVE: Numerous studies have shown that lead and cadmium are multi-target toxicants, but little is known about the effects of these two metals in mixture, especially on the immune cells [1,2]. HL-60 cells and Jurkat cells were used as models to explore the single and combined cytotoxic effect of lead and cadmium on immune cells. Also, the genotoxic potential of each individual metal was analyzed.

METHODS: Lead (10-100 μM) and cadmium (2.5-10 μM) were introduced individually and as mixtures in cell lines for 24 hours. The concentrations of Pb and Cd for the analysis of mixture interaction were selected from their individual cytotoxic effects. The effect additivity method was utilized, in which concentration of each compound, equivalent to its IC_{20}, was calculated from single metal response curve [3]. For the assessment of cytotoxicity, cells were incubated for 2 hours with Presto blue reagent and the absorbance was measured at 570 nm. Statistical analysis was performed according to Student's t-test; p values below 0.05 were considered significant. To determine genotoxicity of Pb and Cd, indirect immunofluorescence method with primary anti-phospho-hystone H2A.X antibody was used. The genotoxic effects were evaluated by the chi-square test; p values below 0.05 were considered significant.

RESULTS: Lead and cadmium caused cytotoxic effects in both cell lines. Cadmium exhibited higher cytotoxic potential. The most pronounced cytotoxic effect was observed at the lowest concentrations of metals (2.5 μM for cadmium and 25 μM for lead). Further increase in metal concentration did not lead to proportional decline in cell viability, in both lines, respectively. Metal mixtures showed synergistic effect in HL-60 cells and antagonistic effect in Jurkat cells, compared to individual metals. Cadmium exhibited a more potent genotoxic effect than lead, and showed dose dependence in both cell lines.

CONCLUSIONS: The combined effects should be considered in the risk assessment of heavy metal toxicity.

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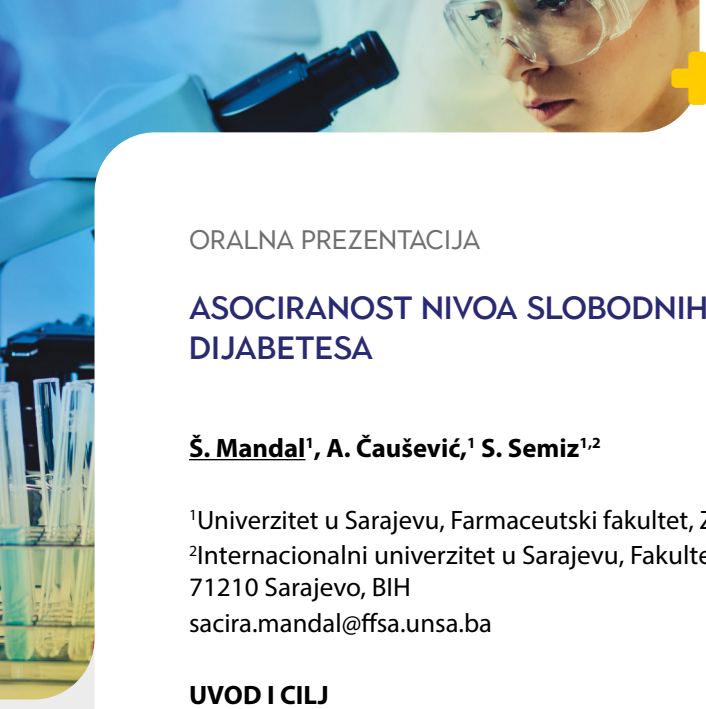
KEY WORDS: metal mixtures, cytotoxicity, genotoxicity, HL-60 cells, Jurkat cells



ORALNA PREZENTACIJA

ASOCIRANOST NIVOA SLOBODNIH MASNIH KISELINA I BILIRUBINA KOD TIP 2 DIJABETESA

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UVOD I CILJ

Serumske koncentracije bilirubina pokazuju antilipolitički efekat na metabolizam slobodnih masnih kiselina (SMK), a postoje i indicije da nivo SMK interferira sa metabolizmom bilirubina (1). Nedavna studija su pokazale da je bilirubin reverzibilno vezan uz endotelnu disfunkciju uzrokovanu djelovanjem povišenog nivoa SMK i da su povišene koncentracije ovih metabolita signifikatno povezane sa rizikom razvoja Tipa 2 dijabetesa (T2D) (2). Cilj ove studije je bilo ispitati potencijalnu asociranost serumskih koncentracija SMK i bilirubina kod pacijenata oboljelih od T2D.

METODE

U ovoj studiji je bilo uključeno 109 ispitanika, od toga 54 kontrole, i 55 T2D pacijenta, oba spola i različite starosne dobi. Nivo bilirubina je određen na hemijskom analizatoru VITROS 350, a SMK gasnom hromatografijom uz maseni spektrometar kao detektor.

REZULTATI

Poređenjem biohemijskih parametara između kontrolne grupe ispitanika i T2D pacijenata pokazana je signifikatna razlika u nivou glukoze, glikiranog hemoglobina (HbA1c), bilirubina, lipidnog profila (holesterol, triglicеridi, HDL), starosne dobi, miristinske kiseline (C14:0) i gama-linolenske kiseline (C18:3) ($p<0.05$).

ZAKLJUČCI

Povišene koncentracije bilirubina i SMK različite dužine lanca i stepena zasićenosti povezani su razvojem T2D i mogu se primjeniti kao potencijalni biomarkeri i terapijske mete u terapiji T2D.

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KLJUČNE RIJEČI :bilirubin, slobodne masne kiseline, tip 2 dijabetes

ASSOCIATION OF LEVELS OF FREE FATTY ACIDS AND BILIRUBIN WITH TYPE 2 DIABETES

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INTRODUCTION AND OBJECTIVE

Serum bilirubin concentrations show antilipolytic effect on free fatty acid metabolism (FFA), and there are indications that FFA levels interfere with bilirubin metabolism (1). Recent study have reported that bilirubin is reversibly linked to endothelial dysfunction caused by elevated FFA levels and that elevated concentrations of these metabolites are significantly associated with the risk of developing Type 2 Diabetes (T2D) (2). The aim of this study was to examine the potential association of serum concentrations of FFA and bilirubin with T2D.

METHODS

In this study, we recruited 109 subjects, 54 controls and 55 T2D patients, adjusted for age and gender. Bilirubin level was determined by using the chemical analyzer VITROS 350, while FFA levels were analyzed by gas chromatography with mass spectrometer as a detector.

RESULTS

Our results showed a significant difference in levels of glucose, glycated hemoglobin (HbA1c), bilirubin, lipid profile (cholesterol, triglycerides, HDL), myristic acid (C14: 0) and gamma-linolenic (C18: 3) between T2D patients and control subjects ($p<0.05$).

CONCLUSIONS

It appears that elevated levels of bilirubin and FFA of different chain lengths and degrees of saturation are associated with the development of T2D and could be used as potential T2D biomarkers and therapeutic targets.

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KEYWORDS :bilirubin, free fatty acids, type 2 diabetes

ORALNA PREZENTACIJA

LIJEK-LIJEK-GEN INTERAKCIJE CITOHROMA CYP2C19

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UVOD I CILJ

Interakcije lijekova smatraju se najčešćim uzrokom neželjenih efekata lijekova. Farmakokinetičke metaboličke lijek-lijek interakcije najčešći su tip interakcija (1). Lijek-lijek-gen interakcije (LLGI) su kompleksne interakcije koje ovise o genetici pacijenta. Citohrom 2C19 je važan enzim koji učestvuje u metabolizmu heterogene skupine lijekova uključujući inhibitore protonske pumpe (IPP), antidepresive, benzodiazepine i klopidogrel (2). Citohrom 2C19 je podložan genetičkim polimorfizmima. Osim toga, mnogo lijekova inducira ili inhibira CYP2C19, što povećava mogućnost nastanka interakcija.

Cilj je istražiti dostupne podatke o LLGI preko CYP2C19 kao i zvanične smjernice za primjenu saznanja o ovim interakcijama u kliničkoj praksi.

METODE

Pretraživana je PubMed baza podataka. Uključeni su originalni i revijalni naučni radovi o lijek-lijek-gen interakcijama preko CYP2C19 enzima objavljeni do augusta 2018. godine.

REZULTATI

Interakcije preko CYP2C19 imaju različitu kliničku značajnost. IPP kompetitivnom inhibicijom smanjuju aktivaciju klopidogrela kod normalnih (NM) i ultrabrzih (UM) metabolizera, ali ne i sporih (PM) metabolizera. Oralni kontraceptivi inhibiraju metabolizam omeprazola kod NM, ne i kod UM. Sultiam zbog inhibicije CYP2C19 izaziva rast koncentracije aktivnog metabolita klobazama kod NM i IM. Rifampicin znatno smanjuje koncentraciju mefenitoina kod NM zbog indukcije CYP2C19. Interakcije su dodatno kompleksne kada lijek ima više od jednog metaboličkog puta. Koncentracija takrolimusa jako raste pri istovremenoj primjeni sa itrakonazolom i vorikonazolom kod PM za CYP2C19 zbog inhibicije CYP3A4 preko kojeg se takrolimus metabolizira.

ZAKLJUČCI

Genetički polimorfizmi mogu pojačati intenzitet interakcija između lijekova. CYP2C19 metabolizira često korištene lijekove i zbog toga je važno znati kako ovaj enzim sudjeluje u nastanku klinički važnih interakcija. Ovo može dovesti to efikasnije terapije i smanjenja incidence neželjenih efekata lijekova koji se metaboliziraju ovim enzimom.

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KLJUČNE RIJEČI: metabolizam, CYP2C19, lijek-lijek-gen interakcije, genetički polimorfizmi

DRUG-DRUG-GENE INTERACTIONS OF CYTOCHROME CYP2C19

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INTRODUCTION AND OBJECTIVE

Drug interactions are considered as one of the main causes for adverse drug effects. Pharmacokinetic metabolic drug-drug interactions are the most common type of interactions. Drug-drug-gene interactions (DDGI) are complex type of interactions which depend on the patient genetics. CYP2C19 is an important enzyme which metabolizes many different drug groups, including proton pump inhibitors (PPIs), antidepressants, benzodiazepines and clopidogrel. Cytochrome 2C19 is subject to genetic polymorphisms. Also many drugs induce or inhibit CYP2C19, which increases possibility of drug-drug interactions.

The objective is explore DDGI which include CYP2C19 as well as current guidelines for implementing knowledge about these interactions in clinical practice.

METHODS

We explored PubMed database. Original papers and reviews about drug-drug-gene interactions that involve CYP2C19 published before August 2018 were included.

RESULTS

Interactions which include CYP2C19 are of different clinical importance. PPIs cause competitive inhibition thus decreaseing activation of clopidogrel in normal (NM) and ultra-fast metabolizers (UM) for CYP2C19, but not in poor (PM) metabolizers. Oral contraceptives inhibit metabolism of omeprazole in NM, but not in UM. Sulthiame inhibits CYP2C19 and therefore increases plasma concentration of active metabolite of clobazam in NM and IM. Rifampicin substantially decreases plasma concentration of mephenytoin in NM because of CYP2C19 induction. These interactions are aditionally complex if a drug uses more than one metabolic pathway. Plasma concentration of tacrolimus rises dramatically when administered concomitantly with itraconazole or voriconazole in PM for CYP2C19 because of inhibition of CYP3A4 which metabolizes tacrolimus.

CONCLUSIONS

Genetic polymorhisms can increase magnitude of drug interactions. As CYP2C19 metabolizes commonly used drugs, it is important to know how this enzyme mediates occurence of clinically important interactions. This can lead to more efficient therapy and reduction of the incidence of adverse events of drugs metabolized by this enzyme.

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KEY WORDS: metabolism, CYP2C19, drug-drug-gene interactions, genetic polymorphisms

POSTER

STERN-VOLMER JEDNAČINA U ODREĐIVANJU INTERAKCIJE GENTAMICINA I HUMANOG SERUMA ALBUMINA U BLAGOM DENATURISANOM STANJU

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UVOD I CILJEVI

Humani serumski albumin (HSA) je globularni protein, i jedan od najzastupljenijih proteina krvne plazme. Vezivanje lijeka za HSA značajno utiče na farmakokinetiku lijeka zbog povećavanja topljivosti lijeka u plazmi, smanjenja toksičnosti i zaštite lijeka od oksidacije [1]. Cilj ovog rada jeste ispitivanje interakcija između gentamicina i HSA pri različitim uslovima, na koji način promjena pH utiče na interakciju HSA i gentamicina, te na Ksv konstantu.

METODE

U radu je korištena fluorescentna spektroskopija i Stern-Volmerov pristup za analizu stepena gašenja fluorescence [2 i 3]. Fluorescentni spektri su snimljeni za uzorke gentamicina tri različita proizvođača, pet različitih koncentracija i dvije vrijednosti pH (6,5 i 7,4), u prisustvu i odsustvu 2M uree.

REZULTATI

Prema dobivenim rezultatima, veće koncentracije lijeka dovode do jačeg vezivanja na HSA. Snažnija interakcija bila je između gentamicina i HSA pri pH 7,4. Interakcije između gentamicina i HSA pri pH 7,4, tj. u fiziološkim uslovima, kao i pri pH 6,5 ovise o koncentraciji lijeka. Snažnije vezivanje lijeka na HSA dovodi do smanjenja koncentracije slobodnog lijeka u krvnoj plazmi. Konstanta vezivanja, Ksv izračunata je na osnovu intenziteta fluorescence na 340 nm, koristeći Stern-Volmerovu jednadžbu. Modificirani oblik Stern-Volmerove jednačine je korišten za određivanje konstante asocijacije kao i broja vezivnih mjesta na molekuli HSA. Interakcija između HSA i gentamicina smanjena je u blago denaturirajućem stanju HSA (2M urea), posebno pri pH 6,5.

ZAKLJUČAK

Na osnovu Stern-Volmerove jednačine dobivene su neznatne razlike u vrijednostima Ksv, pri pH 6,5 odnosno 7,4. Međutim, koristeći modificiranu Stern-Volmer-ovu jednačinu, dobivene su značajne razlike za konstante Ka i n pri različitim pH vrijednostima.

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KLJUČNE RIJEČI: humani serumski albumin, gentamicin, Stern-Volmerova jednačina, konstanta gašenja fluorescence, konstanta asocijacije

STERN-VOLMER EQUATION IN DETERMINATION OF INTERACTION BETWEEN GENTAMICIN AND HUMAN SERUM ALBUMIN AT MILD DENATURED CONDITION

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INTRODUCTION AND OBJECTIVE

Human serum albumin (HSA) is a globular protein and one of the most abudant protein in human blood plasma. Binding of a drug molecule to HSA significantly affects the pharmacokinetics of the drug as it increases drug solubility in plasma, decreases toxicity and protects molecules from oxidation [1]. The aim of this work was to determine the interactions between gentamicin and HSA at different conditions, and on which way change of pH affects on HSA ability to bind gentamicin and K_{sv} constant.

METHODS

This study was made using fluorescence spectroscopy and the Stern-Volmer approach for analysing fluorescence quenching [2 i 3]. Fluorescence spectra were recorded for three different gentamicin brands at five different concentrations, and two pH values (6.5 and 7.4), in the presence and absence of 2 M urea.

RESULTS

According to the obtained results, higher drug concentrations leads to stronger quenching to HSA. The interaction between gentamicin and HSA were stronger at pH 7.4. Additionally, the interactions between gentamicin brands and HSA at pH 7.4, i.e. at physiological conditions, as well as at pH 6.5 depends on drug concentration,. Higher level of drug binding to HSA, leads to lower concentration of a free drug in blood plasma. The binding constant, Ksv was calculated based on fluorescence intensity at 340 nm using the Stern-Volmer equation. We used a modified form of the Stern-Volmer equation to determine the association constants as well as the number of binding sites on the HSA molecule. The interaction between HSA and gentamicin decreased at mild denaturated state (2 M urea), especially at pH 6.5.

CONCLUSIONS

Based on the Stern-Volmer equation, insignificant differences in Ksv values were obtained at pH 6.5 and 7.4. However, significant differences were obtained for the constants, Ka and n for different pH values, using the modified Stern-Volmer equation.

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KEY WORDS: Human serum albumin, gentamicin, Stern-Volmer equation, fluorescence quenching constant, association constant

POSTER

MOŽDANI NATRIURETSKI PEPTID (BNP) I N-TERMINALNI PRO-MOŽDANI NATRIURETSKI PEPTID (NT-proBNP) KOD BOLESNIKA SA SRČANIM ZATAJENJEM

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UVOD I CILJ

Prema smjernicama Europskog kardiološkog društva natriuretski peptidi (BNP i NT-proBNP) koriste se za razlikovanje srčanog zatajenja od ostalih patoloških stanja sa sličnim simptomima [1]. Cilj ovog istraživanja je usporediti koncentracije BNP-a i NT-proBNP-a s obzirom na vrstu srčanog zatajenja.

METODE

Ovo istraživanje uključivalo je 50 ispitanika. Ispitana je povezanost BNP-a i NT-proBNP-a sa dobi, spolom, vrstom srčanog zatajenja. Koncentracije BNP-a određene su kemiluminiscentnom imunokemijskom metodom (CMIA) na analizatoru Abbott Architect 2000i, a koncentracije NT-proBNP-a elektrokemiluminiscentnom metodom (ECLIA) na analizatoru Roche Cobas e 411. Podaci su statistički obrađeni u MedCalc Software's VAT Version 19.0.7.

REZULTATI

Najveće koncentracije BNP-a i NT-proBNP-a su bile u dobnoj skupini od 69-83 godine (P<0,001), dok povezanost natriuretskih peptida i spola nije dokazana. Povezanost između koncentracije BNP-a i NT-proBNP-a je bila statistički značajna (P<0,001, rho=0,88). U ispitanika sa kroničnim srčanim zatajenjem (KSZ) su izmjerene značajno veće koncentracije NT-proBNP-a (P<0,001) i BNP-a (P=0,002) u odnosu na ispitanike s akutnim srčanim zatajenjem (ASZ) što je u skladu s ranijim istraživanjima [2]. Koncentracija BNP-a je 3 puta, a NT-proBNP-a 6,5 puta veća u KSZ u odnosu na ASZ. Vrijednosti medijana sa interkvartilnim rasponom prikazane su u Tablici 1.

Tablica 1. *Koncentracije natriuretskih peptida u kroničnom i akutnom srčanom zatajenju.*

Varijable		Kronično srčano zatajenje	Akutno srčano zatajenje
Koncentracija (medijan, IQR)	BNP (pg/mL)	1305,7 (1071,0 - 2349,0)	421,5 (237,0 – 1069,6)
	NT-proBNP (pg/mL)	16171,5 (11813,0 – 30372,0)	2463,0 (1426,0 – 5176,5)

ZAKLJUČCI

Rezultati ovog istraživanja pokazuju da su koncentracije BNP-a i NTproBNP-a međusobno povezane i da rastu sa životnom dobi bolesnika. Koncentracije BNP-a i NT-proBNP-a su značajno veće u skupini ispitanika s KSZ u odnosu na one s ASZ. Radi duljeg vremena poluraspada, bolje stabilnosti u plazmi te nekoliko puta veće koncentracije od BNP-a u KSZ, NT-proBNP se preferira u dijagnozi i praćenju srčanog zatajenja.

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[2] Ewald B, Ewald D, Thakkinstian A, Attia J. Meta-analysis of B type natriuretic peptide and N terminal pro B natriuretic peptide in the diagnosis of clinical heart failure and population screening for left ventricular systolic dysfunction. Intern Med J. 2008;38:10113

KLJUČNE RIJEČI: Srčano zatajenje, BNP, NT- proBNP, CMIA, ECLIA

BRAIN NATRIURETIC PEPTID (BNP) AND N-TERMINAL PRO-BRAIN NATRIURETIC PEPTID (NT-proBNP) IN PATIENTS WITH HEART FAILURE

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INTRODUCTION AND OBJECTIVE

According to the guidelines of the European Society of Cardiology, natriuretic peptides (BNP and NT-proBNP) are used to distinguish heart failure from other pathological conditions with similar symptoms [1]. The aim of this study is to compare BNP and NT-proBNP concentrations considering the type of heart failure.

METHODS

This study included 50 subjects. The association of BNP and NT-proBNP with age, sex, and type of heart failure was examined. BNP concentrations were determined by the chemiluminescent microparticle immunoassay (CMIA) on an Abbott Architect 2000i analyzer, and NT-proBNP concentrations by the electrochemiluminescent method (ECLIA) on a Roche Cobas e 411. The data were statistically analyzed using MedCalc Software's VAT Version 19.0.7.

RESULTS

The highest concentrations of BNP and NT-proBNP were in the 69-83 age group (P <0.001), while the association between natriuretic peptides and sex has not been established. The association between BNP concentration and NT-proBNP was statistically significant (P <0.001, rho = 0.88). Significantly higher concentrations of NT-proBNP (P <0.001) and BNP (P = 0.002) were measured in subjects with chronic heart failure (CHF) compared with subjects with acute heart failure (AHF), which is consistent with earlier research [2]. The concentration of BNP is 3-fold and NT-proBNP is 6.5-fold higher in CHF compared to AHF. The values of the median with the interquartile range are shown in Table 1.

Table 1. *Concentrations of natriuretic peptides in chronic and acute heart failure.*

Variables		Chronic heart failure	Acute heart failure
Concentration (median, IQR)	BNP (pg/mL)	1305,7 (1071,0 - 2349,0)	421,5 (237,0 – 1069,6)
	NT-proBNP (pg/mL)	16171,5 (11813,0 – 30372,0)	2463,0 (1426,0 – 5176,5)

CONCLUSIONS

The results of this study show that the concentrations of BNP and NTproBNP are interrelated and increase with the age of the patient. BNP and NT-proBNP concentrations were significantly higher in the CHF subjects compared with those with AHF. Due to its longer half-life, better plasma stability, and several times higher concentrations than BNP in CHF, NT-proBNP is preferred in the diagnosis and monitoring of heart failure.

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KEYWORDS: Heart failure, BNP, NT- proBNP, CMIA, ECLIA

POSTER

EVALUIRANJE BRZOG TESTA ZA DETEKCIJU PSIHOAKTIVNIH SUPSTANCI TESTNIM TRAKAMA POREĐENJEM SA TEHNIKOM MULTIPLICIRANOG IMUNOODREĐIVANJA (EMIT)

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UVOD I CILJEVI

Zloupotreba psihoaktivnih supstanci u stalnom je porastu kako u svijetu tako i u Bosni i Hercegovini [1,2]. U ovom istraživanju evaluirane su testne trake u skriniranju psihoaktivnih supstanci poređenjem sa EMIT metodom. Ovim metodama detektirane su psihoaktivne supstance kanabinoidi, opijati i benzodiazepini. Ispitivanje se radilo na dvije grupe ispitanika, 40 ispitanika na kliničkom tretmanu odvikavanja i 40 ispitanika studentske populacije.

METODE

Detekcija kanabinoida, opijata i benzodiazepina u urinu obje grupe ispitanika rađena je sa dvije metode: testom brze detekcije pomoću trakica i tehnikom multipliciranog imunoodređivanja (EMIT), kao najčešće korištenom metodom [3]. Detekcija je rađena po protokolu EMIT ® II Plus imunoeseja i po protokolu gabControl ® testnih trakica na kanabinoide, opijate i benzodiazepine, a uzete su iste granične vrijednosti detekcije za obje metode.

REZULTATI

U obje ispitivane grupe prilikom testiranja tetrahidrokanabinola i opijata nije bilo ispitanika koji su bili pozitivni EMIT metodom, a negativni testnim trakama niti obrnuto. U grupi ispitanika na kliničkom tretmanu odvikavanja 4 ispitanika su bila pozitivna na tetrahidrokanabinol, dok su u studentskoj populaciji svi ispitanici bili negativni. U grupi ispitanika na kliničkom tretmanu odvikavanja 9 ispitanika je bilo pozitivno na opijate, dok su u studentskoj populaciji svi ispitanici bili negativni. Kod testiranja na benzodiazepine, došlo je do odstupanja u rezultatima dobivenim sa dvije metode u grupi ispitanika na kliničkom tretmanu odvikavanja i u grupi ispitanika studentske populacije.

ZAKLJUČAK

Prema očekivanjima u grupi ispitanika na kliničkom tretmanu odvikavanja detektovano je prisutvo psihoaktivnih supstanci. Nije bilo odstupanja rezultata dobijenih testnim trakama od rezultata dobijenih EMIT II Plus esejom kod detekcije kanabinoida i opijata u obje grupe ispitanika. Pri detekciji benzodiazepina u urinu, u obje grupe ispitanika došlo je do odstupanja rezultata dobijenih testnim trakama od rezultata dobijenih EMIT metodom.

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KLJUČNE RIJEČI: tetrahidrokanabinol, opijati, benzodiazepini, enzimska višestruka imunotehnika, EMIT ® II Plus imunoesej, gabControl ® testne trakice.

EVALUATION OF A RAPID PSYCHOACTIVE SUBSTANCE DETECTION TEST USING TEST STRIPS BY COMPARING IT WITH THE MULTIPLE IMMUNOASSAY TECHNIQUE (EMIT)

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INTRODUCTION AND OBJECTIVES
Psychoactive substances abuse is on the rise, both globally and in Bosnia and Herzegovina [1,2]. In this study, test strips for psychoactive substance screening were evaluated by comparison with the EMIT method. The presence of psychoactive substances cannabinoids, opiates, and benzodiazepines, was detected using these methods. The study was conducted on two groups of subjects, 40 subjects on clinical treatment of withdrawal and 40 subjects in the student population.

METHODS
The detection of cannabinoids, opiates, and benzodiazepines in the urine of both groups of subjects was performed using two methods: rapid detection test with strips and the Multiple Immunoassay (EMIT) technique, as commonly used method [3]. Detection was performed using the EMIT® II Plus immunoassay protocol and the gabControl® test strips for cannabinoids, opiates, and benzodiazepines, and the same cutoff values for detection were taken for both methods.

RESULTS
In both groups, tested for tetrahydrocannabinol and opiates, there were no subjects who tested positive by the EMIT method, and negative by test strips or vice versa. In the withdrawal clinical treatment group, 4 tested positive for tetrahydrocannabinol, while in the student population, all tested negative. In the withdrawal clinical trial group, 9 subjects tested positive for opiates, while in the student population, all subjects tested negative. When testing for benzodiazepines, there were discrepancies in the results obtained using two methods in both tested groups.

CONCLUSION
The presence of psychoactive substances was detected in a group of subjects on clinical withdrawal treatment. There was no discrepancy between the results obtained by the test strips and EMIT immunoassay in the detection of cannabinoids and opiates in both groups of subjects. In the detection of benzodiazepines, in both groups of subjects there was a deviation of the results obtained by test strips from the results obtained by the EMIT method.

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KEY WORDS: tetrahydrocannabinol, opiates, benzodiazepines, enzyme multiple immunotechnics, EMIT® II Plus immunoassays, gabControl® test strips.

POSTER

UTICAJ BETAMETAZON DIPROPIONATA NA AKTIVNOST ENZIMA KATALAZE U *IN VITRO* USLOVIMA

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UVOD I CILJ

Većina farmaceutskih i nutritivnih spojeva plasiraju se na tržište kao inhibitori enzima. Takvi inhibitori pokazuju svoje specifično djelovanje u inhibiciji enzima unutar stanica, bakterija, virusa, životinjskih biljaka i ljudskog tijela. Od njihovog otkrića, liječenje kortikosteroidima je jedan od najčešće korištenih i učinkovitih tretmana za različite upalne i autoimune poremećaje. Hipoteza je da kortikosteroidi djeluju inhibitorno na enzim katalazu, budući da posjeduju antiupalno i imunosupresivno djelovanje. Cilj ovog istraživanja jeste odrediti tip inhibicije, kinetičke konstante i ispitati uticaj kortikosteroida betametazon dipropionata na aktivnost katalaze u *in vitro* uslovima.

METODE

Korištena je spektrofotometrijska metoda zasnovana na praćenju reakcije sa vodik peroksidom kao susptratom. Nakon inkubacije na 37°C nagrađen je stabilni kompleks dodatkom amonij heptamolibdata i analizirani su signali.

REZULTATI

Dobiveni rezultati ukazuju na akompetitivni tip inhibicije kod betametazon dipropionata na osnovu čega je potvrđena hipoteza. Primjenom Lineweaver-Burk-ove jednačine izračunate su vrijednosti kinetičkih parametara maksimalne brzine (V_{max}) i Michaelis-Menten-ove konstante (K_m) koje opadaju uz povećanje koncentracija betametazon dipropionata. Najveći procenat inhibicije prisutan je pri koncentraciji betametazon dipropionata od 33,81 µM.

ZAKLJUČCI

Istraživanje je pokazalo da enzim katalaza slijedi Michaelis-Menten-ov kinetički model. Na osnovu grafičkog prikaza uticaja betametazon dipropionata očigledno je da se radi o akompetitivnom tipu enzimske inhibicije, na što ukazuju paralelni pravci za različite koncentracije betametazon dipropionata. Povećanjem koncentracija supstrata sama reakcija stvaranja kompleksa (enzim/supstrat) odvija se znatno većom brzinom nego pri manjim koncentracijama supstrata. Betametazon dipropionat u *in vitro* uslovima inhibira katalazu i utiče na njenu aktivnost pri različitim koncentracijama, što ukazuje na to da pri ispitivanim koncentracijama supstrata ispoljava poboljšano antiupalno djelovanje.

KLJUČNE RIJEČI: betametazon dipropionat, katalaza, enzimska inhibicija, spektofotometrija.

THE EFFECT OF BETAMETHASONE DIPROPIONATE ON CATALASE ACTIVITY *IN VITRO*

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INTRODUCTION AND OBJECTIVE
Most pharmaceutical and nutritional compounds are marketed as enzyme inhibitors. Such inhibitors show their specific action in inhibiting enzymes within cells, bacteria, viruses, animal plants and the human body. Since their discovery, corticosteroid treatment has been one of the most commonly used and effective treatments for various inflammatory and autoimmune disorders. The hypothesis is that corticosteroids have an inhibitory effect on the enzyme catalase, since they have antiinflammatory and immunosuppressive effects. The aim of this study is to determine the type of inhibition, kinetic constant and to examine the effect of corticosteroids betamethasone dipropionate on catalase activity *in vitro*.

METHODS
A spectrophotometric method based on monitoring the reaction with hydrogen peroxide as a substrate was used. After incubation at 37 ° C, the stable complex was rewarded with the addition of ammonium heptamolybdate and the signals were analyzed.

RESULTS
The results obtained indicate an acompetitive type of inhibition in betamethasone dipropionate, which confirmed the hypothesis. Using the Lineweaver-Burk equation, the values of kinetic parameters of maximum velocity (V_{max}) and Michaelis-Menten constant (K_m) were calculated which decrease with increasing concentrations of betamethasone dipropionate. The highest percentage of inhibition was present at a betamethasone dipropionate concentration of 33.81 μM.

CONCLUSIONS
Research has shown that the catalase enzyme follows Michaelis-Menten's kinetic model. Based on the graphical representation of the effect of betamethasone dipropionate, it is evident that this is an acompetitive type of enzymatic inhibition, as indicated by parallel directions for different concentrations of betamethasone dipropionate. By increasing substrate concentrations, the complex formation reaction (enzyme/substrate) itself proceeds at a much higher rate than at lower substrate concentrations. Betamethasone dipropionate inhibits catalase *in vitro* catches and affects its activity at different concentrations, suggesting that it exhibits improved antiinflammatory activity at test substrate concentrations.

KEY WORDS: betamethasone dipropionate, catalase, enzymatic inhibition, spectrophotometry

POSTER

KONCENTRACIJA CISTATINA C U SERUMU ZDRAVE NOVOROĐENČADI DO TRI DANA STAROSTI

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UVOD I CILJ

U kliničkoj praksi koncentracija serumskog kreatinina se koristi kao pokazatelj bubrežne funkcije iako je dokazano da ovaj marker nije pouzdan iz više razloga. S druge strane studije su pokazale da je Cistatin C (Cys C) puno bolji pokazatelj bubrežne funkcije kod ispitanika starijih od jedne godine jer ne ovisi o dobi, spolu i mišićnoj masi. [1, 2] Budući da nema dovoljno podataka o Cys C za novorođenačku populaciju glavni cilj ovog rada je odrediti raspon koncentracije Cys C kod zdrave novorođenčadi, starosti 1 – 3 dana.

METODE

U istraživanje je bilo uključeno 77 zdrave novorođenčadi starosti 1-3 dana. Ispitanici su bili podijeljeni prema spolu, dužini, tjelesnoj masi i koncentraciji CRP. Koncentracija Cys C u serumu je određena turbidimetrijskim imunokemijskim testom na lateks česticama (PETIA) , Abbott Architect 8200ci. Podaci su statistički obrađeni u MedCalc Software's VAT Version 19.0.7.

REZULTATI

U istraživanje je bilo uključeno 77 zdrave novorođenčadi od čega je 49 muškog i 28 ženskog spola prosječne starosne dobi od 2 dana. Najviše novorođenčadi je imalo Apgar 10 (69/77). Prosječna težina novorođenčadi je iznosila 3,15 ±0,55 kg, medijan dužine novorođenčadi 0,55 (53-56) cm, medijan koncentracija CRP-a 3,0 (1,45-6.15) mg/L, a medijan koncentracije Cys C 2,05 (1,84-2,27) mg/L. Nije utvrđena povezanost koncentracije Cys C sa spolom, dužinom, tjelesnom masom, dobi, niti sa koncentracijom CRP-a.

ZAKLJUČCI

Medijan vrijednost za koncentracije serumskog Cys C u ovom istraživanju je iznosila 2,05 (1,84-2,27) mg/L kod zdrave novorođečadi u dobi do 3 dana. Naši rezultati pokazuju da koncentracija Cys C ne ovisi o spolu, dužini, tjelesnoj masi, dobi, niti o koncentraciji CRP-a. Budući da Cys C ne prolazi posteljicu, trebao bi biti prvi test izbora za procjenu bubrežne funkcije u prvim danima života.

LITERATURA

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KLJUČNE RIJEČI: novorođenče, Cistatin C**,** serum, PETIA metoda

SERUM CONCENTRATION OF CYSTATIN C IN HEALTHY NEWBORNS AGED 1 TO 3 DAYS

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INTRODUCTION AND OBJECTIVE

In clinical practice, serum creatinine concentration is used as an indicator of renal function although this marker has been shown to be unreliable for several reasons. On the other hand, studies have shown that Cystatin C (Cys C) is a much better indicator of renal function in subjects older than one year because it does not depend on age, sex and muscle mass. [1,2] Since there is insufficient data on Cys C for the newborn population, the main objective of this study is to determine the Cys C concentration range in healthy infants, 1-3 days old.

METHODS

The study included 77 healthy newborns 1-3 days old. The newborns were divided according to gender, length, body weight, age and CRP concentration Serum Cys C concentration was determined by particle-enhanced turbidimetric immunoassay assay (PETIA) on Abbott Architect 8200ci. Data were statistically analyzed by MedCalc Software's VAT Version 19.0.7.

RESULTS

The study included 77 newborns, of which 49 were male and 28 were female, and the average age was 2 days. The most newborns had Apgar 10 (69/77). The average newborn weight was 3.15 ± 0.55 kg, the median newborn length was 55 (53-56) cm, and the median CRP concentration was 3.0 (1,45-6.15) mg/L. The median concentration of Cys C was 2.05 (1.84-2.27) mg/L. No correlation was found between Cys C concentrations and gender, length, body weight, age, or CRP concentration.

CONCLUSIONS

The median serum Cys C concentration in this study was 2.05 (1.84–2.27) mg/L in healthy newborns up to 3 days old. Our results show that Cys C concentration does not depend on sex, length, body weight, age, or CRP concentration. As Cys C does not pass the placenta, it should be the first choice among tests of renal function in the first days of life.

LITERATURE

[1] Justin T. Kastl. Renal function in the fetus and neonate Seminars in Fetal & Neonatal Medicine (2017) 1-7.
[2] Edit Muhari-Stark, Gilbert J. Burckart Glomerular Filtration Rate Estimation Formulas for Pediatric and Neonatal Use,J Pediatr Pharmacol Ther. 2018; 23(6):424–431.

KEYWORDS: newborn, cystatin C, serum, PETIA method

POSTER

BIOHEMIJSKI TESTOVI VS MALDI-TOF-MS

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UVOD I CILJ

Industrijska mikrobiologija se susreće sa većim zahtjevima kada je riječ o identifikaciji mikroorganizama. Cilj rada je dokazati visok stupanj pouzdanosti masene spektrometrije u odnosu na biohemijske testove.

METODE

Za poređenje ove dvije metode identifikacije korišteni su in-house mikroorganizmi iz proizvodnih pogona, kolonije iz uzoraka nesterilnih formi lijekova sa kazein soja digestivnog agara i standardi mikroorganizama.

REZULTATI

Pregledom rezultata korištenih metoda uočljivo je da biohemijski sistemi nude više od jednog rezultata sa različitim procentima pouzdanosti, dok se masenom spektrometrijom najčešće dobije jedan rezultat sa visokim procentom pouzdanosti. Masenim spektrometrom je postignuta tačna identifikacija do nivoa vrste za sve aplicirane standarde mikroorganizama sa procentom pouzdanosti od 99,9% izuzev *Bacillus subtilis* koji je identifikovan sa procentom 50%. Reproducibilnost, ispitana na osam mikroorganizama, je iznosila 100% za sve mikroorganizme osim za rod *Bacillus*, a ponovljivost na dva ispitana mikroorganizma je iznosila 100%. Na osnovu urađenih testova u ovom radu evidentno je da maseni spektrometar, koji koristi MALDI-TOF tehnologiju (engl. *Matrix Assisted Laser Desorption Ionization Time-of-Flight*), ima višestruke prednosti u odnosu na biohemijske testove: moguća je analiza 192 uzorka tokom jednog pokretanja aparata, vrijeme potrebno za analizu uzorka je manje od 5 minuta, baza podataka je veća od one kod biohemijskih testova uz mogućnost nadograđivanja, na tržištu su dostupni reagensi spremni za upotrebu, čitav proces je automatizovan sa već pripremljenim slijedom rada i osoblje je lakše educirati za rad.

ZAKLJUČCI

Biohemijski testovi, pored vremena koje iziskuju, nisu dovoljno pouzdani i svaka nedoumica prilikom rasta mikroorganizma, vodi nedoumicama pri odabiru vrste testa, što samo širi spektar rezultata, umjesto da ga sužava. Uvođenjem masene spektrometrije u rutinsku mikrobiološku analizu identifikacije postignuta je značajna optimizacija procesa mikrobiološke analize.

KLJUČNE RIJEČI: kontrola kvaliteta, farmaceutska mikrobiologija, identifikacija mikroorganizama, biohemijski testovi, masena spektrometrija

BIOCHEMICAL-BASED PHENOTYPING VS MASS SPECTROMETRY

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INTRODUCTION AND OBJECTIVE
Industrial microbiology is faced with new requests regarding microbial identification. We compared the performances of two systems: one based on MALDI-TOF MS and one based on biochemical testing.

METHODS
To compare these two methods in identification, we used environmental strains, strains from non-sterile solid oral dosage forms cultivated on Tryptic Soy Agar and standard strains.

RESULTS
Overviewing the results, it is evident that biochemical systems always offer more than one result with different confidence values, while mass spectrometry mostly gives one result with high confidence value. Mass spectrometry correctly identified to the species level all applied standard strains with confidence value of 99,9%, except *Bacillus subtilis* which is identified with confidence value of 50%. Reproducibility, examined on eight microorganisms is 100% except for genus *Bacillus*. Repeatability, examined on two microorganisms is 100%.
Based on the peformed tests it is evident that mass spectrometry, which uses MALDI-TOF technology (Matrix Assisted Laser Desorption Ionization Time-of-Flight), has multiple advantages compared to biochemical tests: 192 isolates can be tested per run, time for analysis is less than 5 minutes per sample and the database is significantly wider than the ones for biochemical tests with an upgrade option. Ready-to-use reagents are available on the market and all process is automated with pre-created workflow and a user-friendly software.

CONCLUSIONS
In addition to the time they require, biochemical tests are not reliable enough. Any doubt regarding the growth of the microorganism can lead to a longer list of results, rather than shortening it. Introduction of this rapid technology into microbiological identification means improvement and significant process optimization.

KEY WORDS: quality control, pharmaceutical microbiology, microbial identification, biochemical methods, mass spectrometry

HEMIJA I ANALITIKA LIJEKOVA

UVODNO PREDAVANJE

PROCEDURA CERTIFIKACIJE: 25 GODINA USPJEŠNOG RADA

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UVOD I CILJ

Procedura "Certifikacija o pogodnosti substanci monografijama Evropske farmakopeje " je ustanovljena 1994. godine. Prema ovoj proceduri, Certifikacijski Odjel Evropskog Direktorata za Kvalitet Lijekova i Zaštitu Zdravlja (EDQM) izdaje Certifikat o pogodnosti substance monografiji Evropske farmakopeje (CEP) proizvođačima substanci za farmaceutsku upotrebu, ukoliko dokažu da je kvalitet substance kontroliran u skladu sa odgovarajućom važećom monografijom Evropske farmakopeje [1].

Ciljevi prezentacije su predstaviti ulogu i mjesto procedure Certifikacije u Evropskom regulatornom okviru i izvan istog, sa informacijama kako podnijeti zahtjev i kako dobiti CEP.

Ukratko će biti predstavljeno deset najčešćih nedostataka u dokumentaciji o kvalitetu hemijskih substanci sa kojima se susrećemo nakon inicijalne evaluacije dokumentacije novih CEP aplikacija. Kako treba tumačiti informacije predstavljene na CEP-u sa praktičnim primjerima je veoma značajan segment za podnosioce zahtjeva za dobijanje dozvole za stavljanje lijeka u promet koji koriste CEP kako bi zamjenili odgovarajući dio o kvalitetu CTD dosjea [3], i biti će predmetom ove prezentacije.

METODE

Prezentacija se bazira na primjeni ICH I EU vodiča i zahtjeva za kvalitet substanci za farmaceutsku upotrebu.

KLJUČNE BROJKE

Od 1994 godine zaprimljeno je oko 7000 CEP aplikacija (za > 1000 različitih substanci), a trenutno je važećih oko 5000 CEP-ova. Kada je riječ o CEP-ovima, svake godine EDQM zaprimi oko 300 novih aplikacija i oko 1800 zahtjeva za reviziju CEP-ova .

ZAKLJUČCI

Iskustvo stečeno u proteklih 25 godina je pokazalo da je procedura Certifikacije definitivno uspješna "priča": CEP-ovi su prihvaćeni i koriste se u zemljama potpisnicama Konvencije o elaboraciji Evropske farmakopeje (38), kao i sve veći broj regulatornih tijela izvan Europe (npr. Kanada, Australija, Singapur, WHO, Južna Afrika, itd…).

REFERENCE

[1] Resolution AP-CSP (07) 1 on the 'Certification of Suitability to the Monographs of the European Pharmacopoeia (Revised Version)' (Adopted by the Public Health Committee (CD-P-SP) on 21/02/2007); http://www.edqm.eu;

[2] Top ten deficiencies (2015-2016) – CEPs for chemical purity (PA/PH/CEP (16) 58, December 2016); http://www.edqm.eu;

[3] Guideline 'How to read a CEP' (PA/PH/CEP (15) 31, April 2018); http://www.edqm.eu

KLJUČNE RIJEČI: EDQM, CEP, top ten deficiencies

THE CERTIFICATION PROCEDURE: 25 YEARS OF SUCCESSFUL STORY

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INTRODUCTION AND OBJECTIVE

The procedure for 'Certification of Suitability to the monographs of the European Pharmacopoeia' was established in 1994. The manufacturers of substances for pharmaceutical use can provide proof that the quality of the substance is suitably controlled by the relevant monographs of the European Pharmacopoeia by means of a certificate of suitability (CEP) granted by the Certification Department of the European Directorate for the Quality of Medicines & HealthCare (EDQM) [1].

The objectives of this presentation is to give an overview of the role and place of the Certification procedure in the European regulatory framework and beyond, with information on how to apply and obtain a CEP. The top ten most frequent questions raised after the initial assessment of new applications for Certificates of Suitability (CEP) for chemical substances is briefly presented [2]. Also, as very important point for the Marketing Authorisation applicants who are using CEPs to replace the respective quality part of the CTD dossier, discussion with practical examples is given on how the information reported on the CEP is to be interpreted [3].

METHODS

Presentation will refer to ICH and EU requirements and quality guidelines for pharmaceutical substances.

KEY FIGURES

Since 1994, around 7000 CEP applications have been received (for > 1000 different substances), and there are currently around 5000 valid CEPs. Each year ~300 new applications and ~1800 revisions of CEPs are submitted to the EDQM.

CONCLUSION

Experience gained over 25 years has shown that the CEP procedure is definitely a successful story: CEPs are widely accepted in Ph. Eur. Convention member states (38) and increasing number of authorities outside Europe have decided to accept CEPs to support their work (e.g. Canada, Australia, Singapore, South Africa, WHO, etc.)

REFERENCES

[1] Resolution AP-CSP (07) 1 on the 'Certification of Suitability to the Monographs of the European Pharmacopoeia (Revised Version)' (Adopted by the Public Health Committee (CD-P-SP) on 21/02/2007); http://www.edqm.eu;

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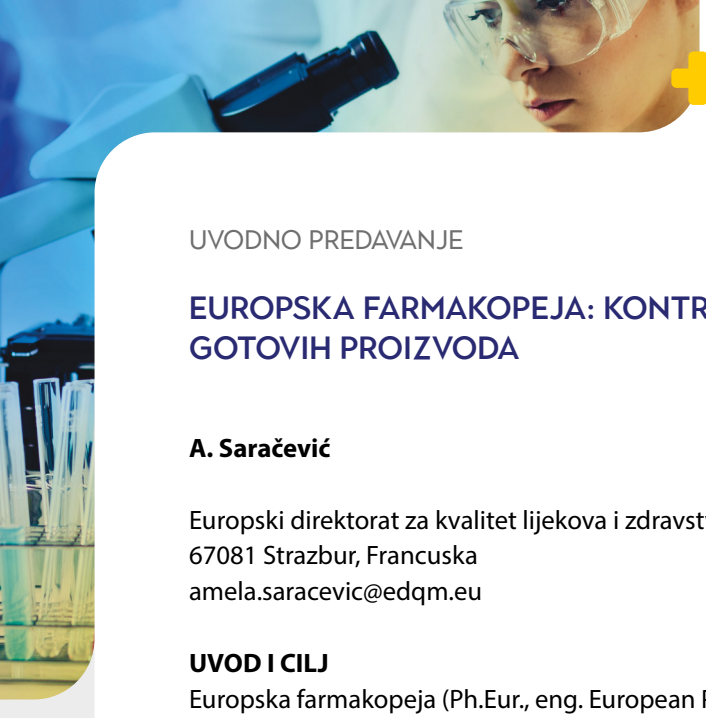
[3] Guideline 'How to read a CEP' (PA/PH/CEP (15) 31, April 2018); http://www.edqm.eu;

KEY WORDS: EDQM, CEP, top ten deficiencies



UVODNO PREDAVANJE

EUROPSKA FARMAKOPEJA: KONTROLA ONEČIŠĆENJA I MONOGRAFIJE GOTOVIH PROIZVODA

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UVOD I CILJ

Europska farmakopeja (Ph.Eur., eng. European Pharmacopoeia) je službena referenca za kontrolu kvaliteta lijekova i njihovih komponenti. Sadrži oficijelne standarde koji pružaju pravnu i naučnu osnovu za kontrolu kvaliteta tokom procesa razvoja, proizvodnje i stavljanja lijeka u promet. Jedan od ključnih elemenata u osiguranju kvaliteta lijekova i njihovih komponenti jeste kontrola onečišćenja. U Ph.Eur., kontrola onečišćenja je obuhvaćena općom monografijom *Supstance za farmaceutsku upotrebu (2034)*, nekoliko općih poglavlja i tekstova, poput *5.10.*, te metodama navedenim u individualnim monografijama.

Posljednjih godina, Komisija za Ph.Eur. je odlučila započeti elaboraciju monografija za gotove proizvode koji sadrže hemijski definisane aktivne supstance, kao odgovor na potrebe svojih korisnika. Cilj rada je predstaviti okvir za kontrolu onečišćenja u Ph.Eur., kao i nedavni razvoj monografija za gotove proizvode.

REZULTATI

Sekcija *Onečišćenja* u monografiji sadrži onečišćenja, koja su uglavnom organskog porijekla, za koja se zna da mogu biti detektovana metodama propisanim u monografiji. Prema općoj monografiji *2034*, ako drugačije nije propisano ili obrazloženo i odobreno, organska onečišćenja u aktivnim supstancama moraju se prijaviti, identificirati, kad je to moguće, i kvalificirati, kada su prisutna iznad praga kvalifikacije [1].

Onečišćenja opisana u monografijama gotovih proizvoda uključuju degradaciona onečišćenja koja nastaju tokom proizvodnje i roka trajanja gotovog proizvoda, uključujući i sintetska onečišćenja koja su ujedno i degradacioni produkti [2].

ZAKLJUČCI

Rad Ph.Eur. u oblasti kontrole onečišćenja je kontinuiran proces i profil onečišćenja obuhvaćen nekom monografijom odražava postojeće puteve sinteze koji su odobreni od strane regulatornih tijela. Isto tako, monografije gotovih proizvoda se elaboriraju tako da uzimaju u obzir trenutna naučna saznanja i relevantne lijekove koji su trenutno odobreni na tržištu. U obje navedene oblasti, uspostavljeni mehanizam revizije monografija osigurava da Ph.Eur. standardi kvaliteta ostanu transparentni i naučno utemeljeni, sa robusnim, validiranim i dostupnim metodama ispitivanja/specifikacijama koje pomažu u zaštiti javnog zdravlja osiguravajući da su lijekovi na tržištu prihvatljive kvalitete.

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KLJUČNE RIJEČI: monografija, kontrola onečišćenja, gotovi proizvodi

EUROPEAN PHARMACOPOEIA: CONTROL OF IMPURITIES AND MONOGRAPHS ON FINISHED PRODUCTS

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INTRODUCTION AND OBJECTIVE

The European Pharmacopoeia (Ph.Eur.) is an official reference for the quality control of medicines and their components. The official standards published therein provide a legal and scientific basis for quality control during the development, production and marketing processes. One of the key elements in assuring quality of medicines and their components is the control of impurities. In the Ph.Eur., control of impurities is covered by the general monograph *Substances for pharmaceutical use (2034)*, several general chapters and texts, such as *5.10.*, and test(s) given in the individual monographs.

In recent years, the Ph. Eur. Commission has decided to start elaborating monographs on finished products (FPs) containing chemically defined active substances (APIs), in response to needs of its users. The objective is to present the framework of impurities' control of the Ph.Eur. and recent developments of monographs on FPs.

RESULTS

The *Impurities* section in a monograph includes impurities, which are usually organic, that are known to be detected by the tests prescribed in the monograph. According to the general monograph *2034*, unless otherwise prescribed or justified and authorised, organic impurities in APIs are to be reported, identified, wherever possible, and qualified when present above the qualification threshold [1].

Impurities described in the FP monographs include degradation impurities arising during manufacture and shelf-life of the FP, including those impurities of synthesis that are also degradation products [2].

CONCLUSIONS

The work of Ph.Eur. on controlling impurities continues and the impurity profiles covered by the monographs reflect the existing routes of synthesis approved by the competent authorities. Likewise, FP monographs are elaborated to take into account current scientific knowledge and relevant medicinal products authorised at present. For both, the revision mechanism in place ensures that Ph.Eur. quality standards remain transparent and scientifically sound, with robust, validated and affordable testing methods/specifications that help to protect public health, by ensuring that medicines are of an acceptable quality.

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KEY WORDS: monograph, impurity control, finished products

UVODNO PREDAVANJE

IZ SVETA DOPINGA — MALE TAJNE MELDONIJUMA

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UVOD I CILJ

Meldonijum kao lek pokazuje kardioprotektivne i antiishemijske efekte. Usled potencijalnog efekta na poboljšanje performansi u sportu Svetska antidoping agencija ga je dodala 2016 godine na listu zabranjenih supstanci [1]. Cilj ove studije bio je da se uradi karakterizacija izlučivanja meldonijuma putem urina nakon višestruke parenteralne primene i na taj način utvrdi koliko dugo je moguće odrediti koncentraciju meldonijuma u urinu.

METODE

Za analizu je korišćen system Aria Transcend TLX-1 LC povezan sa TSQ Vantage triple quadrupol detektorom. Za hromatografsku analizu korišćena je silika predkolona u kombinaciji sa Atlantis HILIC kolonom. Mobilna faza A sastojala se od vode sa 0,2%-tnom formijatnom kiselinom a mobilna faza B sastojala se od metanola sa 0,1% -tnom mravljom kiselinom. Protok mobilne faze bio je 0,4 mL min^{-1} uz sledeći gradijent: 100% B (0–1 min), 0%–40% B (1-5 min), 40% B (5-7 min), 100% B (7-11 min).

REZULTATI

Validacija LC/MS/MS metode urađena je u skladu sa smernicama Svetske antidoping agencije. Validirana metoda primenjena je za određivanje meldonijuma u urinu 6 volontera nakon višestruke parenteralne primene. Na osnovu dobijenih rezultata izračunati su farmakokinetički parametri. Dobijene vrednosti za alfa poluživot bile su 1,4 h, za beta 9,4 h i za gama 655 h čime se pokazuje da trokompartmentski model najbolje opisuje farmakokinetiku leka.

ZAKLJUČCI

U ovom radu urađena je karakterizacija izlučivanja meldonijuma putem urina nakon višestruke parenteralne primene. Utvrđeno je da je poluvreme eliminacije meldonijuma 24-36 dana uz mogućnost detektovanja meldonijuma više meseci nakon višestruke parenteralne primene. Po prvi put je pokazano da se eliminacija meldonijuma putem urina može opisati trokompartmentskim modelom.

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KLJUČNE REČI: meldonijum; doping kontrola, farmakokinetika; eliminacija putem urina

FROM DOPING WORLD — SMALL SECRETS OF MELDONIUM

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INTRODUCTION AND OBJECTIVE

Meldonium is a drug exhibiting cardioprotective and anti-ischemic effects. Due to its potential performance-enhancing benefit in sports, meldonium was added to the World Anti-Doping Agency (WADA) list of prohibited substances in 2016 [1]. The objective of the study was to characterize the pharmacokinetic urinary excretion pattern of meldonium when administered as multiple injections and in this way to define how long it is possible to determine meldonium in urine.

METHODS

The samples were analyzed using an Aria Transcend TLX-1 LC system interfaced to a TSQ Vantage triple quadrupole. A silica precolumn was used and the HPLC column was an Atlantis HILIC Silica. Mobile phase A consisted of water with 0.2% of formic acid, and mobile phase B consisted of methanol with 0.1% formic acid. A constant flow rate of 0.4 mL min^{-1} was applied with the following gradient: 100% B (0–1 min), 0%–40% B (1-5 min), 40% B (5-7 min), 100% B (7-11 min).

RESULTS

Validation of the LC/MS/MS procedure was performed according to WADA guidelines. The validated method was applied for the determination of the concentration of meldonium in urine samples from six volunteers after multipledose parenteral application of meldonium injections. On the basis of the obtained results, pharmacokinetic parameters were calculated. A three-compartment model was found to best describe the pharmacokinetics of meldonium with average alpha, beta, and gamma half-lives of 1.4 hours, 9.4 hours, and 655 hours, respectively.

CONCLUSIONS

In this study, the urinary excretion pattern of meldonium in six healthy volunteers was characterized after multiple parenteral application of the drug. A terminal half-life of 24-36 days was demonstrated, allowing meldonium to be detected in urine for several months after administration. It was shown, for the first time, that the observed excretion profiles of meldonium in urine can be adequately described by a three-compartment model.

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KEY WORDS: meldonium; doping analysis; pharmacokinetics; urinary excretion

UVODNO PREDAVANJE

DOPRINOS BORBI PROTIV DOPINGA U BIH: DESET GODINA OD OSNIVANJA AGENCIJE ZA ANTIDOPING KONTROLU BIH

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UVOD I CILJ

Agencija za antidoping kontrolu Bosne i Hercegovine je utemeljena Zakonom o sportu Bosne i Hercegovine kojeg je donijela Parlamentarna skupština BiH 2008. godine. Prve doping kontrole urina pod nadležnošću Agencije su obavljene 2010. godine. Agencija posjeduje status "Code compliance" i svu prateću regulativu izdatu od strane Svjetske antidoping agencije (*World Anti-Doping Agency*-WADA). U 2019. godini Agencija je otpočela sa programom biološkog pasoša sportiste (*Athlete Biological Passport*-ABP).

METODE

Analizirani su podaci o broju uzoraka urina, kao i pozitivnih doping slučajeva prikupljeni u humanom i animalnom sportu.

REZULTATI

Agencija je 2010. godine prikupila samo 72 uzorka urina te ih analizirala u akreditovanoj laboratoriji u Bukureštu. Trenutno, Agencija prikuplja godišnje oko 400 uzoraka urina i 40 uzoraka krvi. Doping kontrola u periodu 2010.-2018. među bosanskohercegovačkim sportistima pokazala je prisustvo dopinga u slijedećim sportovima: kick boks, dizanje tegova, karate, rukomet, kajak, košarka. Supstance koje su detektovane kod sportista su: boldenon, methandienon, amfetamin, metamfetamin, THC, efedrin, diuretici. U periodu 2011.-2012. Agencija je prikupila 15 uzoraka u konjičkom sportu gdje je bilo 3 pozitivna slučaja, kao i jedno odbijanje kontrole, što je takođe sankcionisano kao pozitivan slučaj. Zabranjene supstance koje su nađene u testiranim uzorcima konja su: triamcinolon-acetonid, fenilbutazon, teofilin, deksametazon.

ZAKLJUČAK

Pojedini sportovi imaju povećan rizik od zloupotrebe zabranjenih supstanci. Procenat doping pozitivnih slučajeva među bosanskohercegovačkim sportistima se kreće između 1-1.5%, što je u skladu s globalnom prevalencom dopinga. Nađeno je 20% doping pozitivnih uzoraka testiranih u konjičkom sportu, te bi se na ovaj problem trebalo ukazati odgovornim osobama u konjičkom sportu u BiH.

KLJUČNE RIJEČI: doping, Svjetska antidoping agencija, agencija.

CONTRIBUTION TO FIGHT AGAINST DOPING IN BOSNIA AND HERZEGOVINA: TEN YEARS OF ESTABLISHING AGENCY FOR ANTI-DOPING CONTROL OF B&H

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INTRODUCTION AND OBJECTIVE
Agency for anti-doping control of Bosnia and Herzegovina was established in accordance with the Law on sports by the parliamentary assembly of Bosnia and Herzegovina in 2008. First doping controls of urine of Bosnian athletes under legislative of the Agency started in 2010. The Agency has Code compliance with all regulating documents issued by World Anti-Doping Agency (WADA). Also Athlete Biological Passport (ABP) program started in 2019.

METHODS
Data about the number of samples collected by the Agency and number of positive doping cases in human and animal sports were analyzed.

RESULTS
In 2010 the Agency collected only 72 urine samples and analyzed them for doping substances in accredited laboratory in Bucharest. Nowadays Agency collects around 400 samples per year and 40 samples of blood. Doping positive cases in a period 2010-2018 among Bosnian athletes were detected in following sports: kick boxing, weightlifting, karate, handball, kayak; basketball. Substances that had been detected among athletes are: boldenone, methandienone, amphetamine, metamphetamine, THC, ephedrine, diuretics. During the years 2011.- 2012. Agency also collected 15 samples in animal sports, where 3 positive cases were found and one refusal of doping control, which is also sanctioned as a positive case. Forbidden substances found among tested horses are: triamcinolone-acethonide, phenyl-buthasone, teophylline, Dexamethasone.

CONCLUSIONS:
Certain sports have higher risk of forbidden substances abuse among athletes. Percent of doping positive cases among Bosnian athletes was between 1-1.5 %, similar to the global prevalence of doping. We found 20 % of doping positive cases among horse samples, and this problem should be addressed among decision makers in Bosnian animal sport.

KEY WORDS: doping, WADA, Agency.

ORALNA PREZENTACIJA

IN SILICO I *IN VITRO* I ISPITIVANJE ANTI-HIV PROTEAZNE AKTIVNOSTI NOVOSINTETISANIH PROPIOFENONSKIH DERIVATA

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UVOD I CILJ

Otkriće Virusa humane imunodeficijencije (HIV-a) i istraživanje molekularnih mehanizama ključnih za ciklus replikacije virusa dovelo je do identifikacije važnih proteinskih struktura - potencijalnih ciljnih mesta dejstva lekova u terapiji AIDS-a. Jedno od najznačajnijih otkrića je HIV-1 proteaza (PR), enzim koji ima ključnu ulogu u ciklusu replikacije HIV-a [1]. U ovoj studiji posmatrali smo interakcije novosintetisanih propiofenonskih derivata (PD) iz klase halkona (1,3-diaril-2-propen-1-ona) kao i tri komercijalna leka (KL) (lopinavira, ritonavira i darunavira) sa aktivnim mestom PR kao i *in vitro* inhibitorne efekte na samom enzimu.

METODE

U *in vitro* ispitivanju anti-PR aktivnosti pripremani su rastvori PD i KL u DMSO u koncentracionom opsegu od 1000 μM do 0,01 μM. . Inhibicija enzimske aktivnosti praćena je fluorimetrijskom metodom [3]. *Docking* proračuni su vršeni pomoću programa Autodock Vina u 3D strukturi katalitičkog mjesta PR (pdb kod: 6B36). Strukture jedinjenja su generisane i optimizovane pomoću softverskog paketa ChemOffice v7.0.0 Ultra

REZULTATI

In silico studijom od 280 PD selektovano je i sintetisano 20 derivata iz klase halkona koji su pokazali visok afinitet vezivanja za katalitičko mjesto PR. Inhibitorna aktivnost sintetisanih derivata ispitana je *in vitro* na PR. Dobijeni rezultati ukazuju da sva testirana jedinjenja pokazuju inhibitornu aktivnost u koncentracionom opsegu od 1 do 0,1 μM. U poređenju sa rezultatima dobijenim sa komercijalnim jedinjenjima inhibitorna aktivnost je u rangu komercijalnih lekova a za tri ispitivana jedinjenja i bolja.

ZAKLJUČCI

Dobijeni rezultati ukazuju da se sintetisana jedinjenja mogu klasifikovati kao potencijalni inhibitori HIV-1 proteaze. Dalje istraživanje je usmereno na ispitivanju ADMET osobina sintetisanih jedinjenja kao i sintezi njihovih homo analoga za koje su *in silico* ispitivanja takođe pokazala zadovoljavajuće rezultate.

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KLJUČNE RIJEČI: HIV, inhibitori HIV-1 proteaze, molekularni *docking*, halkoni, *in vitro* anti-HIV proteazna aktivnost , fluorescentna spektroskopija

IN SILICO AND *IN VITRO* TESTING OF ANTI-HIV PROTEASE ACTIVITY OF NEWLY SYNTHESIZED PROPIOPHENONE DERIVATIVES

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INTRODUCTION AND THE AIM

The discovery of human immunodeficiency virus *(*HIV) and the investigation of the molecular mechanisms crucial for the viral replication cycle have led to the identification of important protein structures-potential drug target sites for acquired immunodeficiency syndrome (AIDS) therapy. One of the most significant discoveries is HIV-1 protease (PR), an enzyme that plays a key role in the HIV replication cycle [1]. In this study, we observed the interactions of newly synthesized propiophenone derivatives (PD) with chalcone (1,3-diaryl-2-propen-1-one) as the basic structure and three commercial drugs (CD) (lopinavir, ritonavir and darunavir) with the active site of PR, as well as, *in vitro* inhibitory effects on the enzyme itself.

METHODS

In *in vitro* assay of anti-PR activity, PD and CD solutions in dimethylsulfoxide (DMSO) were prepared in a concentration range from 1000 μM to 0.01 μM. Ultra. Enzyme activity inhibition was monitored by the fluorimetric method [1].Docking calculations were performed using Autodock Vina in the 3D structure of the PR catalytic site (pdb code: 6B36). Compound structures were generated and optimized using the ChemOffice v7.0.0 software package.

RESULTS

In silico study of 280 PDs, 20 chalcone class derivatives that showed a high binding affinity for the PR catalytic site were selected and synthesized. The inhibitory activity of the synthesized derivatives was tested in vitro for PR. The results obtained indicate that all tested compounds show inhibitory activity in the concentration range of 1 to 0.1 μM. Compared to the results obtained with commercial compounds, the inhibitory activity is in the activity range of commercial drugs and for the three compounds is even better.

CONCLUSIONS

The obtained results indicate that the synthetised compounds can be classified as potential anti-PR molecules. Further research is aimed at examining the ADMET properties of the synthesized compounds as well as the synthesis of their homo analogues for which *in silico* tests have also shown satisfactory results.

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KEY WORDS: HIV; HIV-1 protease ihibitors; molecular docking; chalcones; *in vitro* anti-HIV protease activity; fluorimetric spectroscopy

ORALNA PREZENTACIJA

UTICAJ RAZLIČITIH TEMPERATURA SKLADIŠTENJA I OTAPALA NA STABILNOST RASTVORA KAPTOPRILA ZA ORALNU UPOTREBU, KONCENTRACIJE 1 MG/ML

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UVOD I CILJ

Značajan problem u liječenju kardiovaskularnih bolesti kod djece je nedostatak industrijski proizvedenih oralnih preparata u nekim zemljama [1]. Ekstemporalni preparati napravljeni u apoteci mogu popuniti ovu prazninu. U ovoj studiji posmatrali smo stabilnost Kaptopril rastvora, koncentracije 1 mg/mL, (rastvarač prečišćena voda i Vit. C amp ili rastvarač 0,1% vodeni rastvor EDTA) čuvani na različitim temperaturama, u cilju pronalaženja mogućnosti za stvaranje stabilnijih rastvora Kaptoprila od onih koji se već koriste u Kliničkoj apoteci KCUS.

METODE ISTRAŽIVANJA

Određivanje sadržaja kaptoprila u rastvorima na dvanaest uzoraka je urađeno spektrofotometrijskom metodom sa maksimalnom apsorpcijm na 327 nm uz slijepu probu. [2] Imajući u vidu da se radi o kompleksnim uzorcima, bilo je potrebno pokazati da ostale supstance u uzorcima ne pokazuju apsoprciju na valnoj dužini produkta reakcije između Kaptoprila i reagensa.

REZULTATI

Sadržaj Kaptoprila ostao je unutar 90% u rastvoru prečišćene vode i Vit. C amp čuvan u frižideru, u odnosu na isti rastvor kaptoprila ako se čuva na + 20 °C (40 %). pH vrijednost za oba rastvora iznosi 5,12 do 5,19. Sadržaj kaptoprila u rastvoru kaptoprila, (rastvarač 0,1% vodeni rastvor EDTA) je 90%, bilo da se čuva na sobnoj temperaturi ili u frižideru. Izmjerena pH vrijednost je 3,3 -3,5 i najsličnija je optimalnoj pH vrijednosti za Kaptopril rastvore, prema literaturnim podacima.

ZAKLJUČAK

Rastvor kaptoprila napravljen od tableta Kaptoprila u rastvaraču prečišćena voda i Vit. C ampula čuvan na + 20 ° bio je stabilan dvije sedmice. Kaptopril u rastvoru 0,1% EDTA-Na bio je stabilan 5 sedmica na 4 ° i 20 ° C.

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KLJUČNE RIJEČI: stabilnost, kaptopril

THE EFFECT OF DIFFERENT STORAGE TEMPERATURES AND SOLVENTS ON THE STABILITY OF CAPTOPRIL SOLUTION, CONCENTRATION 1MG/ML FOR ORAL USE IN CHILDREN

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INTRODUCTION

A significant problem in the treatment of cardiovascular diseases in children is the lack of industrial manufactured oral preparations in the some countries. Extemporaneous compounding preparations can fill this void. It is important for pharmacists to have useful data about the stability of the solutions in order to finding possibilities for making more stable captopril solutions from those already used in the Clinical pharmacy KCUS. Captopril 1 mg/mL oral liquid formulations were prepared from tablets in distilled chemically pure water with the addition of EDTA or of ascorbic acid during 5 weeks. The liquids were stored at 4° and 25 ° C in amber glass bottles.

METHOD

A spectrophotometric method was used having a maximum absorption at 327 nm with a blank test. The determination of the content of captopril was based on twelve comparative solutions. In order to obtain relevant data with the selected method, the absorption spectra were recorded in the range 200-400 nm.

RESULTS

Captopril content was remained to be within the 90% for 5 weeks in the solution of chemically pure water and ascorbic acid when stored in a refrigerator, compared to the same captopril mixture when stored at +20°C (40%). The amount of captopril in captopril solutions in a solution of 0.1% EDTA-Na was remained to be within the 90%, whether stored at room temperature or in a refrigerator and pH value (3,3 -3,5) is similar to the optimum value, according to the literature data.

CONCLUSION

Captopril solutions are more stable if a 0.1% solution of EDTA-Na is used as the solvent instead of vitamin C.

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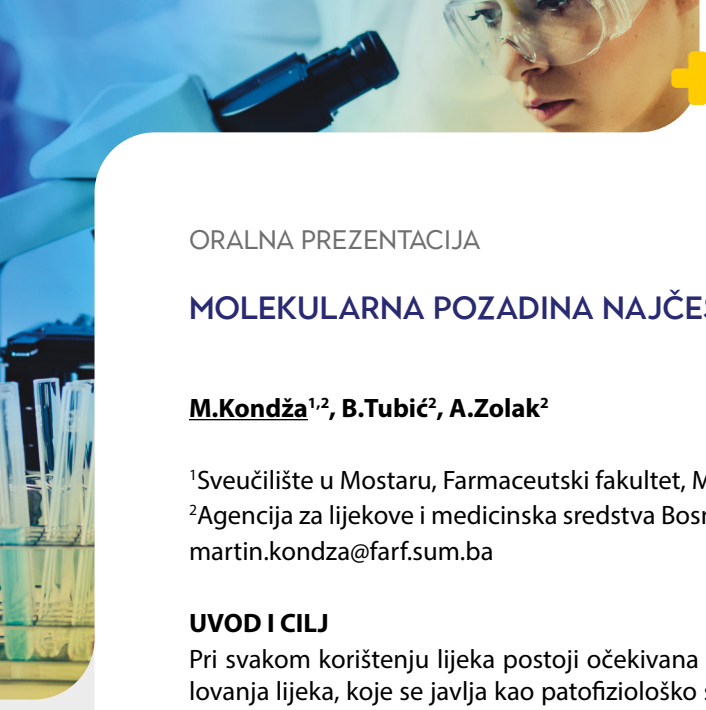
KEY WORDS: stability, captopril



ORALNA PREZENTACIJA

MOLEKULARNA POZADINA NAJČEŠĆIH NUSPOJAVA U BOSNI I HERCEGOVINI

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UVOD I CILJ

Pri svakom korištenju lijeka postoji očekivana mogućnost pojavljivanja nuspojave, odnosno neželjenog djelovanja lijeka, koje se javlja kao patofiziološko stanje ili laboratorijski nalaz uz terapijsku primjenu lijeka. Nadležno tijelo za praćenje nuspojava u Bosni i Hercegovini (BiH) je Agencija za lijekove i medicinska sredstva BiH (ALMBIH). Cilj našeg istraživanja je dati pregled znanstvene literature koja opisuje odabrane nuspojave lijekova na molekularnoj razini, s aspekta biokemije lijekova.

METODE

Pri izradi ovog istraživanja koristili smo se javno dostupnim izvješćima o neželjenim djelovanjima lijekova i medicinskih sredstava ALMBIH-a, te pregledom dostupne znanstvene literature putem *Web of Science* (WoS), platforme u izdanju *Clarivate Analytics* putem koje su dostupne citatne baze koje pokrivaju sva područja znanosti.

REZULTATI

U našem istraživanju usredotočili smo se i istražili sljedeće lijekove i nuspojave: urtikarija uzrokovana jopromidom, anafilaksija uzrokovana oksaliplatinom, smetnje vida uzrokovane ciprofloksacinom, kolitis *Clostridium difficile* uzrokovan ceftriaksonom i gubitak okusa uzrokovan sunitinibom. Pri pretraživanju relevantnih baza uočili smo 14 radova koje opisuju pridruženo neželjeno djelovanje s jopromidom, 63 za oksaliplatin, 86 za ciprofloksacin, 5 za ceftriakson i 1 za sunitinib.

ZAKLJUČCI

Urtikarija tijekom upotrebe jopromida nastaje uslijed aktivacije potkožnog histamina. Oksaliplatin izravno uzrokuje degranulaciju mastocita i bazofila, te posljedični mehanizmi dovode do anafilaksije. Smatra se da destruktivni učinak ciprofloksacina dovodi do razgradnje kolagena i vezivnog tkiva, koji su ključni za integritet staklastog tijela oka. Smanjenje broja bakterija djelovanjem ceftriaksona, pogoduje rastu i razvoju *C. difficile,* što za posljedicu ima pojavu kolitisa.

Dalje ostaje nejasno je li gubitak okusa uslijed korištenja sunitiniba uzrokovan izmjenom receptivnih stanica okusa, izmjenom mirisa preko neurona olfaktornih receptora ili neurodegeneracijom.

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KLJUČNE RIJEČI: Nuspojava, biokemija lijekova, ALMBIH

THE MOLECULAR BACKGROUND OF THE MOST COMMON SIDE EFFECTS IN BOSNIA AND HERZEGOVINA

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INTRODUCTION AND OBJECTIVE
With each use of a drug, there is an expected possibility of a side effect, an undesirable effect of a drug, which occurs as a pathophysiological condition or laboratory finding with the therapeutic use of a drug. The governing authority body for monitoring of adverse drug reactions in Bosnia and Herzegovina (B&H) is the B&H Agency for Medicines and Medical Devices (ALMBIH). The aim of our study is to provide an overview of the scientific literature describing selected side effects of drugs at a molecular level, from the aspect of drug biochemistry.

METHODS
To conduct this research, we used publicly available ALMBIH side effects reports, as well as reviewing available scientific literature through the Web of Science (WoS) platform, a Clarivate Analytics platform through, where citations are available covering all fields of science.

RESULTS
In our study, we focused and investigated the following drugs and side effects: urticaria caused by iopromide, anaphylaxis caused by oxaliplatin, visual impairment caused by ciprofloxacin, colitis *Clostridium difficile* caused by ceftriaxone, and taste loss caused by sunitinib. While searching the relevant databases, we found 14 papers describing the associated adverse reaction with iopromide, 63 for oxaliplatin, 86 for ciprofloxacin, 5 for ceftriaxone, and 1 for sunitinib.

CONCLUSIONS
Urticaria is caused by the activation of subcutaneous histamine during the use of iopromide. Oxaliplatin directly causes mast cell and basophil degranulation, and consequent mechanisms lead to anaphylaxis. The destructive effect of ciprofloxacin is thought to lead to the breakdown of collagen and connective tissue, which are crucial for the integrity of the vitreous body of the eye. The reduction of bacteria by the action of ceftriaxone favors the growth and development of *C. difficile*, resulting in colitis.
It remains unclear whether the loss of taste due to the use of sunitinib is caused by alteration of taste receptor cells, alteration of smell via olfactory receptor neurons, or neurodegeneration.

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KEY WORDS: side effects, drug biochemistry, ALMBIH

POSTER

ADSORPCIJA TETRACIKLIN-HIDROHLORIDA IZ VODENOG RASTVORA NA GRAFEN OKSIDU

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UVOD I CILJ

Grafen predstavlja dvodimenzionalnu strukturu ugljika debljine jednog atoma sa odličnim električnim, optičkim, hemijskim, termalnim i mehaničkim svojstvima [1]. Velika specifična površina (2630 m^2/g), dobra hemijska stabilnost, prisutne funkcionalne grupe, kao i konjugirana π struktura čine materijale na bazi grafena odličnim adsorbensima za različite polutante sa kojima stvaraju jake interakcije [2].

Zbog prekomjerne upotrebe, antibiotici su postali jedni od najčešćih polutanata, a među njima tetraciklini zauzimaju veoma važno mjesto [3], te se stoga sve više pažnje posvećuje tehnikama za njihovu analizu. Cilj ovog istraživanja bio je ispitivanje stepena adsorpcije tetraciklin-hidrohlorida na grafen oksidu kako bi se dobili podaci koji bi u budućnosti mogli poslužiti za razvoj strategije za smanjenje zagađenosti ovim antibiotikom.

METODE

Grafen oksid je sintetiziran modificiranom Hummersovom metodom. Pripremljen je vodeni rastvor tetraciklin-hidrohlorida u koncentraciji 0,01 mg/ml na pH 4. Rastvor je pomiješan sa suspenzijom grafen oksida. Smanjenje sadržaja tetraciklin-hidrohlorida u rastvoru praćeno je pomoću UV-VIS spektrofotometra, mjerenjem apsorbance na dvije talasne dužine (275 nm i 356 nm) tokom 6 sati.

REZULTATI

Nakon miješanja rastvora tetraciklin-hidrohlorida sa suspenzijom grafen oksida, apsorbanca rastvora tetraciklin-hidrohlorida se smanjila . Smanjenje apsorbance dokaz je da je smanjen sadržaj tetraciklin-hidrohlorida, odnosno da je došlo do vezivanja (adsorpcije) tetraciklin-hidrohlorida na grafen oksid. Apsorbanca se smanjivala tokom 6 sati praćenja na obje talasne dužine.

ZAKLJUČCI

U ispitivanim rastvorima došlo je do adsorpcije tetraciklin-hidrohlorida na grafen oksid. Na osnovu navedenog može se zaključiti da grafen oksid ima sposobnost adsorpcije tetraciklin-hidrohlorida pod navedenim uslovima. Ovi rezultati se mogu iskoristiti u budućnosti za analizu grafenskih materijala kao potencijalnih prečišćivača.

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KLJUČNE RIJEČI: grafen oksid, tetraciklin-hidrohlorid, adsorpcija

ADSORPTION OF TETRACYCLINE-HYDROCHLORIDE FROM AN AQUEOUS SOLUTION ONTO GRAPHENE OXIDE

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INTRODUCTION AND OBJECTIVE

Graphene represents one atom thick two dimensional structure of carbon with excellent electrical, optical, chemical, thermal, and mechanical properties [1]. Due to its large surface area (2630 m^2/g), good chemical stability, remaining functional groups and conjugated π structure, graphene materials are excellent adsorbents for different pollutants. They make strong interactions with those pollutants [2].
Antibiotics became one of the most common pollutants because of their excessive use. Tetracyclines took a big part in that [3], and because of that, more and more attention has been paid to the methods for their analysis. The objective of this experiment was to investigate the extent of adsorption of tetracycline-hydrochloride onto graphene oxide. This data could be used to develop strategy for reducing pollution caused by this antibiotic.

METHODS

Graphene oxide was prepared using a modified Hummers method. The concentration of tetracycline-hydrochloride was 0,01 mg/ml, pH of aqueous solution was 4. Solution was mixed with suspension of graphene oxide. UV-VIS spectrophotometer was used to detect the decrease in concentration of tetracycline-hydrochloride in solution by measuring the apsorbance at two wavelengths (275 nm and 356 nm) for 6 hours.

RESULTS

After mixing solution of tetracycline-hydrochloride with suspension of graphene oxide, apsorbance of tetracycline-hydrochloride has been decreased. Decrease in apsorbance is proof that the concentration of tetracycline-hydrochloride has been reduced, in other words, tetracycline-hydrochloride has been adsorbed onto graphene oxide. The apsorbance was decreasing during 6 hours of experiment at both wavelengths.

CONCLUSIONS

In examinated solutions tetracycline-hydrochloride was adsorbed onto graphene oxide. So, it can be concluded that graphene oxide has the capability of adsorption of tetracycline-hydrochloride in these conditions. In future, these results can be used for analysis of graphene materials as potential purifiers.

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KEY WORDS: graphene oxide, tetracycline-hydrocloride, adsorption

POSTER

NAZALNE KAPI - NOVI PRISTUP UJEDNAČENOSTI DOZA

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UVOD I CILJ

Kapi su jedan od najstarijih dozirnih oblika i kao takve su prisutne u većini tečnih farmaceutskih oblika. Međutim, zahtjevi kvaliteta za ujednačenost doza nisu dobro definirani i ujednačeni. Kod kapi za nos, Vodič za kvalitet preparata za inhalaciju i nazalnih preparata Europske agencije za lijekove [1] navodi testove koji moraju biti sastavni dio specifikacije gotovog lijeka, dok u isto vrijeme Europska farmakopeja [2] opisuje samo testove za jednodozne nazalne kapi. U ovom radu ispitan je uticaj variranja površinske napetosti i viskoznosti na ujednačenost doza kapi doziranih kroz različite izvedbe kapaljki.

METODE

Ispitivane su 3 otopine: voda, 0,5% otopina natrij laurilsulfata i 2% otopina hidroksipropilmetilceluloze. Kao dozirni uređaji, korištene su Pasterova pipeta, standardna kapaljka i plastična kapaljka inkorporirana u plastični kontejner komercijalne kapi za nos. Mjerenje variranja doza je vršeno gravimetrijski.

REZULTATI

Evaluacija rezultata u skladu sa Ph.Eur. monografijom 2.9.40 Ujednačenost doznih jedinica [2] je pokazala da od 9 kombinacija dozirni uređaj/otopina, samo su dvije imale prihvatljivu vrijednost < 15. S druge strane, evaluacijom prema propisu za Ujednačenost dostavljenih doza preparata za inhalaciju [2], svaki set rezultata zadovoljava kriterije kvaliteta date u navedenoj monografiji.

ZAKLJUČCI

Visoko variranje rezultata redovno potiče od jednog ili dva mjerenja sa visokim odstupanjem od srednje vrijednosti, dok su ostala mjerenja relativno usko grupisana. Takav rezultat, skupa sa činjenicom da na rezultat ne utiče variranje površinske napetosti i viskoznosti otopine kao ni izvedba mjernog uređaja (kapaljke), navodi na pretpostavku da je uzrok sama procedura manuelnog doziranja. Pretpostavlja se da je sam način korištenja kapaljke kao i variranje u intenzitetu i brzini pritiska glavni uzrok variranja rezultata. To je potrebno imati u vidu prilikom definiranja limita za test ujednačenosti doza kapi za nos, jer je vjerovatno da visoko rasipanje doza ne potiče od osobina same formulacije nego od arhaičnog načina doziranja.

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KLJUČNE RIJEČI: nazalne kapi, ujednačenost dostavljenih doza, ujednačenost doznih jedinica

NASAL DROPS - NEW APPROACH TO DOSE UNIFORMITY

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INTRODUCTION AND OBJECTIVE

Drops are one of the oldest dosage forms and as such, they are present in most liquid pharmaceutical forms. However, the quality requirements for dose uniformity are not well defined and uniform. For nasal drops, the European Medicines Agency's Guideline on the pharmaceutical quality of inhalation and nasal products [1] lists tests that must be an integral part of the finished product specification, while at the same time the European Pharmacopoeia [2] describes only tests for single-dose nasal drops. In this paper, the effect of variation of surface tension and viscosity on the uniformity of droplets dosed through different dropper designs is examined.

METHODS

Three solutions were tested: water, 0.5% sodium lauryl sulfate solution and 2% hydroxypropylmethylcellulose solution. Pasteur pipette, a standard dropper and a plastic dropper incorporated into a plastic container (commercial nasal drops) were used as dosing devices. Dose variation measurements were performed gravimetrically.

RESULTS

Evaluation of results according to Ph.Eur. monograph 2.9.40 The uniformity of dosage units [2] showed that out of the 9 combinations of dosage device / solution, only two had an acceptable value <15. On the other hand, by the evaluation according to the regulation for Uniformity of the delivered doses of inhalation preparations [2], each set of the results meets the quality criteria given in the above monograph.

CONCLUSIONS

High variation in results usually originates from one or two measurements with a high deviation from the mean, while the other measurements are relatively narrowly grouped. Such a result, together with the fact that the result is not affected by the variation of the surface tension and the viscosity of the solution, as well as the performance of the measuring device (droppers), implies that the cause is the manual dosing procedure itself. It is assumed that the use of the dropper itself, as well as variations in the intensity and speed of applied pressure, are the main causes of variation in the results. This should be considered when defining the limit for the test for uniformity of doses for nasal drops, as it is likely that the high dose dissipation does not originate from the properties of the formulation itself but from the archaic dosing method.

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KEY WORDS: nasal drops, uniformity od delivered dose, uniformity of dosage units

POSTER

TEORIJA FUNKCIONALA GUSTOĆE: ANALIZA I PREDVIĐANJE HEMIJSKE REAKTIVNOSTI ZA C-5 SUPSTITUIRANE PIRIMIDINSKE DERIVATE

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UVOD I CILJ

Alkilirajući lijekovi su važna klasa lijekova koji se koriste u liječenju raka, stoga je važno i zanimljivo utvrditi jačinu reakcije alkilirajućih sredstava s DNK bazama [1]. Ova studija predstavlja deskriptore reaktivnosti alkilirajućeg agenasa 2,4-dihloro-5-(2-hloretil)pirimidina (**1**) [2] i njegovog derivata 2,4-dihloro-5-(3-hloropropil) pirimidina (**2**) i uspoređuje ih s 5-fluorouracilom (3) kao lijekom u terapiji.

METODE

Spojevi su podvrgnuti proračunima koristeći teoriju funkcionala gustoće (eng. Density Functional Theory, DFT) s B3LYP baznim setom [3] na nivou 6-31G (d) u programu Spartan 14. Izračunati deskriptori hemijske reaktivnosti su: hemijska tvrdoća (η), elektronički hemijski potencijal (μ) i elektrofilnost (ω).

REZULTATI

Vrijednosti hemijske tvrdoće (η) za spojeve **1**, **2** i **3** iznosile su 2,91 eV, 2,92 eV odnosno 2,71 eV. Što je molekula tvrđa, to je stabilnija/manje reaktivna. Spoj **2** je tvrđi i stoga manje reaktivan od spoja **1** koji je također tvrđi i manje reaktivan od 5-fluorouracila (**3**). Tvrdoća se smanjuje s povećanjem broja alkilnih skupina u bočnom lancu.

Elektronski hemijski potencijal (μ) za spojeve **1**, **2** i **3** iznosio je -4,87 eV, -4,78 eV odnosno -4,09 eV. Što je veći elektronički hemijski potencijal, to je molekula manje stabilna odnosno reaktivnija. Stoga je 5-fluorouracil reaktivniji od **1** i **2**.

Vrijednosti elektrofilnosti pokazuju da je 5-fluorouracil (**3**) (22,57 eV) jači nukleofil od **2** i **1** (33,23 eV, odnosno 34,38 eV). Spojevi **1** i **2** imaju veću sposobnost prihvaćanja elektrona od generičkog elektron donora i, prema tome, bili bi aktivniji prema bazama.

ZAKLJUČCI

Dobiveni rezultati pokazuju da su ispitivane supstance stabilnije/manje reaktivne u odnosu na 5-fluorouracil što može dovesti do slabije aktivnosti, ali i manje nuspojava. Ovi izračunati parametri mogli bi biti korisni u razumijevanju i predviđanju ponašanja strukturno sličnih molekula nepoznate reaktivnosti.

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KLJUČNE RIJEČI: alkilirajući agensi, DFT, deskriptori reaktivnosti

DENSITY FUNCTIONAL THEORY: ANALYSIS AND PREDICTION OF CHEMICAL REACTIVITY FOR C-5 SUBSTITUTED PYRIMIDINE DERIVATIVES

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INTRODUCTION AND AIM

Alkylating drugs are an important class of drugs used in cancer treatment, therefore it is important and interesting to determine the strength of the reaction of the alkylating agents with the DNA bases [1]. This study presents calculated reactivity descriptors for the alkylating agents 2,4-dichloro-5-(2-chloroethyl)pyrimidine (**1**) [2] and its derivative 2,4-dichloro-5-(3-chloropropyl)pyrimidine (**2**) and compare them to 5-fluorouracil (**3**) as the drug in use.

METHODS

Compounds were subjected to calculations using the density functional theory (DFT) with the B3LYP basis set [3] at 6-31G(d) level in the Spartan 14 software. Calculated chemical reactivity descriptors were: chemical hardness (η), electronic chemical potential (μ) and electrophilicity (ω).

RESULTS

Chemical hardness (η) values for compounds **1**, **2** and **3** were 2.91 eV, 2.92 eV and 2.71 eV, respectively. The harder the molecule, the more stable/less reactive it is. Compound **2** is harder and therefore less reactive than compound **1** which is also harder and less reactive than the 5-fluorouracil (**3**). The hardness decreases with the increase in the number of alkyl groups in the side chain.

Electronic chemical potential (μ) for compounds **1**, **2** and **3** were -4.87 eV, -4.78 eV and -4.09 eV, respectively. The greater the electronic chemical potential, the less stable or more reactive is the compound. Therefore, 5-fluorouracil is more reactive than **1** and **2**.

The electrophilicity values indicate that 5-fluorouracil (**3**) (22.57 eV) is a stronger nucleophile than **2** and **1** (33.23 eV and 34.38 eV, respectively). Compounds **1** and **2** have a greater capacity to accept electrons from a generic electron donor and, consequently, they would be more active toward bases.

CONCLUSIONS

Obtained results indicate that studied agents are more stable/less reactive than 5-fluorouracil which might lead to lower activity but also fewer side effects. These calculated parameters could be useful in understanding and predicting the behaviour of structurally similar molecules of unknown reactivity.

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KEYWORDS: alkylating agents, DFT, reactivity descriptors

POSTER

PROCJENA AFINITETA VEZIVANJA SINTETIZIRANOG ACIKLIČKOG NUKLEOZIDNOG ANALOGA I PENCIKLOVIRA S ENZIMOM VAŽNIM ZA REPLIKACIJU *HERPES SIMPLEX* VIRUSA

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UVOD I CILJ

Aciklički nukleozidni analozi sintetički su analozi prirodnih nukleozida u kojima je ciklički šećer zamijenjen acikličkim lancem koji oponaša dio ili cijelu molekulu šećera. Koriste se u terapiji kao moćni antivirusni lijekovi [1], a najpoznatiji su aciklovir, ganciklovir i penciklovir. Sličnost prirodnim nukleozidima omogućava njihovo uklapanje u polinukleotidni lanac, što rezultira prekidom daljnje sinteze polinukleotida ili promjenom funkcije novoformirane nukleinske kiseline.

METODE

In silico doking studija korištena je za procjenu mogućeg načina vezivanja sintetiziranog acikličkog analoga nukleozida 5-(3-hidroksipropil)-N-1-[4-hidroksi-(3-hidroksimetil)butil] pirimidin-2,4-dion-a [2] s timidin kinazom *Herpes simplex* virusa tip 1 (HSV-1 TK) i uspoređivanje s rezultatima za penciklovir. Doking analize omogućile su usporedbu energija vezivanja, inhibicijskih konstanti [Ki], broja vodikovih veza, kao i aminokiselina uključenih u interakciju analiziranih spojeva.

REZULTATI

Energije vezivanja testiranog acikličkog nukleozida i penciklovira s HSV1-TK bile su -2,47 odnosno -4,82 kcal mol^{-1}. Energija vezivanja obrnuto je proporcionalna stabilnosti ispitivanog kompleksa ligand-receptor. Što je energija niža, to je kompleks stabilniji. Konstante inhibicije za aciklički nukleozid i penciklovir iznosile su 15,51 mM odnosno 0,292 mM. Konstanta inhibicije određuje koja je koncentracija spoja potrebna da bi se smanjila maksimalna brzina enzimske reakcije upola. Što je niža inhibicijska konstanta, to je veća inhibicijska aktivnost.

ZAKLJUČCI

Dobiveni rezultati otkrili su moguće hidrofobne interakcije između liganda i receptora. Fosforilacijski esej *in vitro* acikličkog nukleozidnog analoga kao supstrata za HSV-1 TK pokazao je da je slabiji supstrat od lijekova koji su već u upotrebi [2], što ukazuje na dobru korelaciju između *in silico* izračunatih parametara i *in vitro* biološkog ispitivanja inhibicije enzima.

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KLJUČNE RIJEČI: analog acikličkih nukleozida, antivirusni agensi, doking studija

ESTIMATION OF BINDING AFFINITY FOR SYNTHESIZED ACYCLIC NUCLEOSIDE ANALOG AND PENCICLOVIR WITH ENZYME IMPORTANT FOR *HERPES SIMPLEX* VIRUS REPLICATION

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INTRODUCTION AND AIM

Acyclic nucleoside analogues are synthetic analogues of natural nucleosides in which cyclic sugar is replaced by an acyclic chain that mimics part or all of the sugar molecule. They are used in therapy as potent antiviral drugs [1], with aciclovir, ganciclovir, and penciclovir being the most well known. Similarity to natural nucleosides allows them to be incorporated into a polynucleotide chain, which results in interruption of further polynucleotide synthesis or alteration of the function of the newly formed nucleic acid.

METHODS

In silico docking study has been used to estimate possible way of binding of synthesized acyclic nucleoside analog 5-(3-hydroxypropyl)-N-1-[4-hydroxy-(3-hydroxymethyl)butyl] pyrimidin-2,4-dione [2] with thymidine kinase of *Herpes simplex* virus type 1 (HSV-1 TK) and compare the results with penciclovir. Docking analyses provided comparison of binding energies, inhibitory constants [Ki], number of hydrogen bonds, as well as amino acids involved in the interaction of analyzed compounds.

RESULTS

Binding energies of tested acyclic nucleoside and penciclovir with HSV1-TK were -2.47 and -4.82 kcal mol^{-1}, respectively. Binding energy is inversely proportional to the stability of the tested ligand-receptor complex. The lower the energy, the more stable is the complex. Inhibition constants for acyclic nucleoside and penciclovir were 15.51 mM and 0.292 mM, respectively. Inhibition constant determines what concentration of a compound is required to reduce the maximum rate of an enzymatic reaction by half. The lower the inhibition constant, the higher the inhibitory activity.

CONCLUSIONS

Obtained results revealed possible hydrophobic interactions between ligands and receptors. The *in vitro* phosphorylation assay of acyclic nucleoside analog as substrates of HSV-1 TK revealed that it is weaker substrate than drugs already in use [2], indicating good correlation between *in silico* calculated parameters and *in vitro* biological testing of enzyme inhibition.

LITERATURE

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KEYWORDS: acyclic nucleoside analog, antiviral agents, docking study

POSTER

ANTIOKSIDATIVNA AKTIVNOST ŠEST NOVIH ARILMETILEN BIS (3-HIDROKSI-5,5-DIMETIL-2-CIKLOHEKSEN-1-ON) DERIVATA

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UVOD I CILJEVI

Arlmetilen bis (3-hidroksi-5,5-dimetil-2-cikloheksen-1-on) derivati, poznati kao tetraketoni, su prekursori za sintezu heterocikličnih spojeva sa različitim biološkim aktivnostima [1]. Zbog njihove snažne antioksidativne aktivnosti tetraketoni se intenzivno istražuju kao efikasni agensi kod poremećaja povezanih sa oksidativnim stresom poput inflamacije , astme i raka [2]. Osnovni cilj ovog istraživanja je sinteza novih tetraketona i evaluacija njihove antioksidativne aktivnosti.

METODE

Sintetizirana je serija derivata tetraketona **1**-**6** u vodi uz katalizator DABCO, reakcijom Knoevenagel-ove kondenzacije i Michael-ove adicije. Antioksidativna aktivnost je utvrđena primjenom DPPH i FRAP metoda.

REZULTATI

Sintetizirani spojevi su potvrđeni primjenom IR, ^{1}H i ^{13}C NMR spektroskopije, elementarnom mikroanalizom. Evaluacijom antioksidativne aktivnosti utvrđeno je da spoj **4** (dvije hidroksilne grupe u položajima 3 i 4) ima najjači efekat uklanjanja slobodnih radikala, i to IC_{50} je pri koncentraciji 0,0575 mM, a FRAP vrijednost je 50 469,44. Spoj **6** (hidroksilna grupa u položaju 4 i dimetoksi grupe u položajima 3 i 5) ima slabiji efekat uklanjanja slobodnih radikala, i to IC_{50} pri koncentraciji 0,111 mM i FRAP vrijednost 2 417,51. Spoj **2** (dimetoksi grupe u položajima 3 i 4) ima još slabiji efekat uklanjanja slobodnih radikala, i to IC_{50} pri koncentraciji 1,69 mM i FRAP vrijednost 378,09.

ZAKLJUČAK

Dobiveni rezultati upućuju da hidroksilne grupe imaju veću reducirajuću sposobnost i da njihovi položaji imaju snažan efekat na antioksidativnu aktivnost što korelira sa do sada objavljenim rezultatima [3]. Rezultati ovog istraživanja su poticaj za dalje sinteze različitih tetraketona i ispitivanja njihovih bioloških aktivnosti.

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KLJUČNE RIJEČI: Sinteza tetraketona, antioksidativna aktivnost, DPPH, FRAP

ANTIOXIDATIVE ACTIVITY OF SIX NEW ARYLMETHYLEN BIS (3-HYDROXY-5,5-DIMETHYL-2-CYCLOHEXEN-1-ON) DERIVATES

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INTRODUCTION AND OBJECTIVE

Arylmethylen bis (3-hydroxy-5,5-dimethly-2-cyclohexen-1-on) derivates, known as tetraketones, are precursors for synthesis of heterocyclic compoundswith various biological activities [1]. Due their strong antioxidative activity tetraketones have received significant attention as efficient agents against disorders associated with oxidative stress, such as inflammation, asthma and cancer [2]. Primary aim of this study was to synthetize new tetraketones and evaluates their antioxidative activity.

METHODS

Series of tetraketone derivates **1-6** were prepared in aqueous medium with catalyst DABCO via Knoevenagel condensation and Michael addition. Antioxidative activity was measured using DPPH and FRAP methods.

RESULTS

Synthetized compounds were confirmed by IR, ^{1}H and ^{13}C NMR spectroscopy and elemental microanalyses. According to results of antioxidative activity evaluation, compound **4** (two hidroxy groups substituted in positions 3 and 4) has the strongest free radical scavenging effect, IC50 of 0,0575 mM and FRAP value 50469,44. Compound **6** (hydroxy group substituted on position 4 and dimethoxy groups on positions 3 and 5) has lower free radical scavenging effect, IC50 of 0,111 mM and FRAP value 2417,51. Compound **2** (two dimethoxy groups on positions 3 and 4) has lower free radical scavenging effect than previous two, IC50 of 1,69 mM and FRAP value 378,09.

CONCLUSIONS

Obtained results suggested that hydroxy groups have greater reducing power and their positions may have significant effects on the antioxidative activity which is in accordance with previously published data [3]. Results of this study are an incentive for further synthesis of tetraketones with similar structures and evaluation of their biological activities.

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KEY WORDS: tetraketones synthesis, antioxidative activity, DPPH, FRAP

POSTER

POLIVINIL-PIROLIDON UTIČE NA TERMIČKU STABILNOST AMORFNOG INDOMETACINA U ČVRSTIM DISPERZIJAMA

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UVOD I CILJ

Razvoj novih strategija koje se bave problemom rastvorljivosti lijekova je jedan od najvećih izazova u farmaceutskim istraživanjima, uzimajući u obzir da skoro 40% novih sintetisanih lijekova pokazuje slabu rastvorljivost u vodi i slabu bioraspoloživost. Rastvorljivost je značajno poboljšana kada se lijek nalazi u amorfnom stanju, koje je termodinamiči nestabilno zbog viška energije. S druge strane, kristalna forma lijeka je termodinamički stabilna, ali veoma slabo rastvorljiva. Zbog toga je bitno naći način da se stabilizuje amorfna forma a da se pri tome očuva bioraspoloživost i terapeutske karakteristike lijek za vrijeme skladištenja. Jedan od pogodnih načina je disperzija amorfne forme u polimeru[1]. U našoj studiji, ispitivali smo stabilizaciju amorfne forme indometacina dispergovanog u polivinil-pirolidonu PVP. Analiza stabilnosti IMC/PVP je bazirana na kinetičkim parametrima (Ea, ln A i k) i određena termogravimetrijskim tehnikama (TGA).

METODE

Za TGA mjerenja korišten je uređaj Mettler Toledo TGA/DSC 3+, uz prisustvo azota, pri brzini protoka od 80 mL min^{-1} sa sledećim brzinama zagrijavanja, β = 1.25, 2.5, 5, 7.5 and 10°C min^{-1}.

REZULTATI

TG krive čistog indometacina i IMC/PVP sa različitim udjelom IMC (31.5%, 24.3% and 13.8%) su pokazale da se termička stabilnost IMC/PVP poboljšava prilikom povećavanja udjela PVP. Koristeći TGA podatke, kinetički parametri poput Ea, lnA and k su izračunati. Pokazano je da različit udjel PVP u IMC/PVP smješi dovodi do različitog mehanizma termalne dekompozicije IMC u čvrstoj disperziji, ukazujući da sa manjim udjelom PVP razalaganje je stabilisano preko povećanja energetske barijere tj. Ea, dok kod većeg udjela PVP stabilizacija se povećava preko predeksponecijalnog faktora[2].

ZAKLJUČCI

Do sada se smatralo da je uloga polimera u farmaceutskoj formulaciji da poboljša bioraspoloživost bez ikakvog uticaja na termičku stabilnost lijeka. Naša studija je pokazala novi fenomen da povećano prisustvo PVP u čvrstoj disperziji značajno utiče i povećava termičku stabilnost IMC.

LITERATURA

[1] Ben Osman Y, Liavitskaya T, Vyazovkin S. Polyvinylpyrrolidone affects thermal stability of drugs in solid dispersions. International Journal of Pharmaceutics 2018, 551:111-120.
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KLJUČNE RIJEČI: polimer, čvrsta disperzija, kinetika, konstanta brzine, termalna dekompozicija

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POLY(VINYL-PYRROLIDONE) AFFECTS THERMAL STABILITY OF AMORPHOUS INDOMETHACIN IN SOLID DISERSION

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INTRODUCTION AND OBJECTIVE

Development of new formulation strategies capable of overcoming poor drug solubility is a major challenge of the pharmaceutical research, since almost 40% of newly designed drugs show very weak solubility in water and low bioavailability. Solubility is significantly improved when a drug is in an amorphous state, which is thermodynamically unstable due to excess of energy. On the other hand, the crystalline form of a drug is thermodynamically stable, but very poorly soluble. Thus, it is important to find ways to stabilize the amorphous form while maintaing its bioavalilability and therapeutic characteristics during storage. One possible way is to disperse the amorphous form in a polymeric matrix[1]. In our study, we examined stabilization of amorphous form of indomethacin (IMC) via dispersing it in poly(vinylpyrrolidone) (PVP). The stability analysis of IMC/PVP was based on kinetic parameters (Ea, ln A and k) determined by thermogravimetric technique (TGA).

METHODS

The device used for TGA measurements was Mettler Toledo TGA/DSC 3+ instrument, under flow of N_2, at a flow rate 80 mL min^{-1} with the following heating rates, β = 1.25, 2.5, 5, 7.5 and 10°C min^{-1}.

RESULTS

TG curves of neat IMC and IMC/PVP containing different ratio of IMC (31.5%, 24.3% and 13.8%) proved that the thermal stability of IMC/PVP is improved with increasing the content of PVP. By using TGA data, kinetic parameters such as Ea, lnA and k were calculated. It was shown that the use of different content of PVP in IMC/PVP results in different mechanism of thermal decomposition of IMC in the solid dispersion, meaning that decomposition with smaller PVP content is stabilized via increasment in the energy barrier, i.e. activation energy, while at higher content the stabilization occurs via a decrease in the preexponential factor[2].

CONCLUSIONS

So far the role of a polymer in a solid dispersion was considered to be limited to improving bioavailability without having an effect on drug thermal stability. Our study has discovered the novel effect that the thermal stability of IMC in solid dispersions with PVP can be increased significantly with increasing the amount of PVP.

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KEY WORDS: polymer, solid dispersion, kinetics, rate constant, thermal decomposition

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POSTER

USPOREDBA GC METODA ZA ODREĐIVANJE SADRŽAJA ETANOLA U SIRUPU ZA ISKAŠLJAVANJE KORISTEĆI KAPILARNU I PAKOVNU KOLONU

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UVOD I CILJ

Etanol se u sirupima za iskašljavanje određuje gasnom kromatografijom (GC). Cilj rada je razviti dvije metode za određivanje sadržaja etanola koristeći dvije vrste kolona koje se koriste u gasnoj kromatografiji (kapilarana i pakovna), usporediti date rezultate te definisati prednosti i nedostake različitih kolona.

METODE

Razvijene su dvije metode sa uslovima:

Kapilarna kolona:

Stacionarna faza: ZB-624 30 m × 0,53 mm (3,00 µm), gas nitrogen linearna brzina: 36,3 ml/sec, temperatura plameno-jonizacijskog detektora 250°C, tenperatura injektora t=250°C, temperaturni program: temperatura pećnice 40 °C, 7 min, rate 45 °C / min, finalna tempuratura pećnice t=240 °C, 20 min

Pakovna kolona:

Stacionarna faza: Chromosorb 104 (80/100) 2 m x 4 mm, gas nosač: Nitrogen, temperatura injektora t=180 °C; temperatura pećnice, t=220 °C; , temperatura plameno-jonizacijskog detektora t=220 °C, protok 50,0 ml/min;

REZULTATI

Tabela 1. *Prikaz rezultata dobivenih validacijom metoda*

Parametar	Pakovana kolona	Kapilarna kolona
Tačnost **-Bias** **-Recovery**	 -2,7% 97,3% -102,6%	 2,3% 98,4% - 102,3%
Preciznost **-keoficijent varijacije sistema** **-koeficijent varijacije metode** **-granica povjerenja**	 CV=0,9% CV=0,3% CL=0,3%	 CV=0,14% CV=0,38% CL=0,40%
Selektovnost	Nema interferencije	Nema interferencije
Linearnost **-koeficiejnt kolrelacije** **- CV za RF** **-intercept (%)**	 R=0,99936 CV=0,7% 0,7%	 R=0,99981 CV=1,0% -1,8%
Robusnost **-Stabilnost otopine** **-Recovery** **-CV**	 -2,8% -1,0% 97,6%-99,5% 0,8%	 -2,3% - 0,8% 100,3% -100,9% 0,10%-0,23%

ZAKLJUČCI

Dobijeni rezultati su pokazali da su obje metode odgovarajuće za određivanje sadržaja etanola. Kod kapilarne kolone pojavljuje se tailing veći od 2,0 kada kolona izgubi efikasnost nakon velikog broja iniciranja otopine sirupa. Pakovna kolona se pokazala otpornijom na velik broj iniciranja otopine sirupa. Iako se pakovna kolona smatra zastarijelom rezultat je pokazao da je robusnija od kapilarne kolone zbog čega se upotreba smatra opravdanom.

KLJUČNE RIJEČI: kapilarna kolona, pakovna kolona, gasna kromatografija, etanol

COMPARISON OF GC METHODS FOR DETERMINATION OF ETHANOL ASSAY IN COUGH SYRUP USING CAPILLARY AND PACKED COLUMNS

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INTRODUCTION AND OBJECTIVE

Ethanol in cough syrups is determined by gas chromatography (GC). The aim of this paper is to develop two methods for the determination of ethanol assay using two types of columns used in GC (capillary and packed) and to compare obtained results with aim to define advantages and disadvantages of column.

METHODS

Two methods were developed with conditions:

For capillary column:

Stationary phase: ZB-624 30 m × 0,53 mm (3,00 µm), carrier gas nitrogen, linear velocity: 36,3 ml/sec, FID temperature 250°C, injector temperature t=250°C, temperature gradient: oven temperature 40°C, hold 7 min, Rate 45°C/min, Final oven temperature t=240°C, 20 min,

For packed column:

Stationary phase: Chromosorb 104 (80/100) 2 m x 4 mm, carrier gas nitrogen, injector temperature t=180 °C; oven temperature t=220 °C; injector temperature t=220 °C, flow 50,0 ml/min;

RESULTS

Table 1. *Summary of results obtained by validation of both methods*

Parameter	Packed column	Capillary column
Accuracy		
-Bias	-2,7%	2,3%
-Recovery	97,3% -102,6%	98,4% -102,3%
Precision		
- CV of the system	CV=0,9%	CV=0,14%
- CV of the method	CV=0,3%	CV=0,38%
- CL	CL=0,3%	CL=0,40%
Selektovnost	Nema interferencije	Nema interferencije
Linearnost		
- coefficient of correlation	R=0,99936	R=0,99981
- CV for RF	CV=0,7%	CV=1,0%
-intercept (%)	0,7%	-1,8%
Robustness		
- Stability of the solution	-2,8% -1,0%	-2,3% -0,8%
-Recovery	97,6%-99,5%	100,3% -100,9%
-CV	0,8%	0,10%-0,23%

CONCLUSIONS

Obtained redults showed that both methods are appropriate for the determination of ethanol assay in cough syrup. Capillary column show tailing greater than 2.0 when the column loses its efficiency after a large number of syrup solution injections. Packed column proved to be more resistant to the large number of injections of the syrup solution. Although packed column is outdated, it proved to be better and more robust than the capillary column.

KEY WORDS: capillary column, packed column, gas chromatography, ethanol

POSTER

ODREĐIVANJE SADRŽAJA CINKA U UZORCIMA MAGISTRALNO I GALENSKI IZRAĐENE CINKOVE PASTE

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UVOD I CILJ

Cinkova pasta je najzastupljeniji galenski i magistalni preparat cinka koji kao aktivnu komponentu sadrži cink oksid. Izrađuje se kao 25 % pasta cinkovog oksida. Upotrebljava se u liječenju kožnih infekcija, akni, različitih dermatitisa, ali i kao zaštitni premaz kod kožnih iritacija te za zaštitu kože kod pelenskog osipa. Da bi se postigao željeni terapijski efekat svakog lijeka pa tako i cinkove paste, neophodno je da sadrži terapijsku koncentraciju da ne bi došlo do izostanka terapijskog djelovanja [1]. Cilj rada je bio odrediti sadržaj cinka u uzorcima cinkove paste izrađenim u galenskim laboratorijama i apotekama kako bi se utvrdilo da li odgovaraju zahtjevu za kvalitet.

METODE

Određen je sadržaj cinka u šest uzoraka cinkove paste – 3 galenski i 3 magistralno pripremljene cinkove paste. Nakon žarenja odgovarajuće količine uzorka do konstantne mase sadržaj cinka je određen volumetrijski, titracijom sa 0,1 M EDTA uz indikator eriohrocrnoT. Sve analize su rađene u triplikatu.

REZULTATI

Sadržaj cinka niti u jednom analiziranom galenskom uzorku nije odgovarao zahtjevu za kvalitet jer je odstupanje sadržaja bilo iznad dozvoljenog ± 1,5 % u odnosu na deklarisani sadržaj. Sadržaj cink oksida u jednoj magistralno pripremljenoj cinkovoj pasti je odgovarao zahtjevu za kvalitet, dok je u preostala dva analizirana uzorka sadržaj cinka bio izvan granica dozvoljenog odstupanja od ± 1,5 %.

ZAKLJUČAK

Rezultati dobijeni ispitivanjem mogu se smatrati neočekivanim obzirom na jednostavnost izrade cinkove paste. Mogući uzroci odstupanja mogle bi biti greške prilikom vaganja, greške pri izradi, greške u radu analitičara ili neprikladnosti analitičke metode. Radi pouzdanosti dobijenih rezultata, može se preporučiti određivanje cinka metodom atomske spektroskopije, s obzirom na njenu specifičnost i osjetljivost.

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KLJUČNE RIJEČI: cinkova pasta, određivanje sadržaja cinka, kontrola kvaliteta

DETERMINATION OF ZINC CONTENTS IN GALENIC AND EXTEMPORANEOUS SAMPLES

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INTRODUCTION AND OBJECTIVE

Zinc paste is the most common galenic and extemporaneous preparation of zinc, containing zinc oxide as the active component. It is made as a 25% zinc oxide paste. It is used in the treatment of skin infections, acne, various dermatitis, but also as a protective coating for skin irritations and for skin protection in diaper rash. In order to achieve the desired therapeutic effect of each drug, including zinc paste, it is necessary that it contains a therapeutic concentration to prevent the absence of therapeutic action [1]. The aim of the study was to determine the zinc content in zinc paste made in galenic laboratories and pharmacies, to determine if they meet the quality requirement.

METHODS

Zinc content was determined in six samples of zinc paste - 3 galenic and 3 extemporaneous in pharmacy prepared zinc paste. After annealing the appropriate amount of sample to constant mass, the zinc content was determined volumetrically, by titration with 0.1M EDTA with the Eriochrome Black T indicator. All analyzes were performed in triplicate.

RESULTS

The zinc content of the analyzed galenic samples does not meet the quality requirement since the deviation of the content was outside the prescribed ± 1.5% of the declared content. The content of zinc oxide in one extemporaneous prepared zinc paste met the quality requirement, while the content in the other two samples analyzed was outside the tolerance of ± 1.5%.

CONCLUSIONS

The results obtained may be considered unexpected due to the ease of preparation of zinc paste. Possible causes for content deviation could be weighing errors, preparation errors, analyst errors, or inappropriate analytical methods. For the purpose of reliability of the obtained results, it can recommend the determination of zinc by atomic spectroscopy, given its specificity and sensitivity.

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KEY WORDS: zinc paste, determination of zinc content, quality control

POSTER

ISPITIVANJE MOGUĆNOSTI PRIMJENE BILJNIH ULJA U EKSTRAKCIJI FARMACEUTSKI AKTIVNIH SUPSTANCI

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UVOD I CILJ

Ekstrakcija farmaceutskih aktivnih supstanci iz lijekova se provodi primjenom rastvarača kao što su voda, metanol, etanol, metilen hlorid, hloroform i drugi. Svi osim vode su štetni po zdravlje i okoliš pa se danas pokušava naći način za primjenu drugih rastvarača koji će imati istu efikasnost ali manju toksičnost (tzv. „zeleni rastvarači") [1,2]. Biljna ulja posjeduju dvije osobine rastvarača: organske su supstance i ne miješaju se sa vodom. Osnovni cilj istraživanja bio je ispitati mogućnost primjene biljnih ulja kao „zelenih rastvarača" za ekstrakciju.

METODE

Ekstrakcija je provedena na sobnoj temperaturi na dva načina, u lijevku za odvajanje i miješanjem na magnetnoj mješalici. U ispitivanju su korišteni paracetamol i digoksin rastvoreni u vodi, 0,3 M, 1 M i 3 M vodenom rastvoru KCl. Kao rastvarač za ekstrakciju korišteno je suncokretovo ulje. Efikasnost ekstrakcije praćena je spektrofotometrijski mjerenjem apsorbance vodenih otopina u UV području na 244 nm. Efikasnost ekstrakcije određena je na osnovu razlike apsorbanci prije i poslije ekstrakcije.

REZULTATI

Nakon ekstrakcije ispitivanih analita provedene u lijevku za odvajanje nije bilo moguće odvojiti slojeve jer je nastala emulzija. Ekstrakcija miješanjem na magnetnoj mješalici moguća je samo ako se kao rastvarač za analit koristi 0,3 M KCl, pri odnosu analit/ulje 2:1 (V/V), u trajanju od 5 minuta. Pri ovim uslovima ekstrahovano je 16% paracetamola. Procenat ekstrahovanog diazepama, pri istim uslovima, bio je 91%, što bi se moglo objasniti činjenicom da diazepam ima veći logP (logP=3.09) od paracetamola (logP=0.91).

ZAKLJUČAK

Na osnovu dobijenih preliminarnih rezultata može se zaključiti da biljna ulja imaju potencijal za ekstrakciju farmaceutski aktivnih supstanci, posebno onih većim vrijednostima logP.

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KLJUČNE RIJEČI

Extraction, vegetable oils, green solvents

RESEARCH ON POSSIBLE USAGE OF VEGETABLE OILS IN EXTRACTION OF PHARMACEUTICAL ACTIVE SUBSTANCES

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INTRODUCTION AND OBJECTIVE

Extraction of pharmaceutical active substances from medications is achieved with solvents such as water, ethanol, methanol, methylene chloride, chloroform etc. All except water are biohazard, so nowadays we are trying to find a way of usage of alternative solvents that would have same efficiency, but less toxicity (also known as green solvents) [1,2]. Vegetable oils have two characteristics of solvents: they are organic compounds and they do not mix with water. The primary objective of the research was to examine possibility of vegetable oil usage as "green solvents" for extraction.

METHODS

Extraction was conducted on room temperature, in two ways: in separation funnel and mixing in magnetic stirrer. Paracetamol and diazepam, dissolved in water and 0,3M; 1M and 3M KCl-water solution, were used as analytes. Sunflower oil was used as extraction solvent. Extraction efficiency was determined spectrophotometrically by measuring the absorbance of aqueous solutions in UV spectrum at 244 nm. Extraction efficiency was determined based on the difference of absorbance before and after extraction.

RESULTS

After the extraction of examined analytes in separation funnel, it was not possible to separate the layers due to occurred emulsion. The extraction conducted in magnetic stirrer is possible only if we use 0.3M KCl as the solvent for analyte and when the analyte/oil ratio is 2:1 (V/V) in duration of 5 minutes. Under these conditions 16% of paracetamol was extracted. Extracted diazepam percentage, under the same conditions, was 91%, which could be explained by the fact that diazepam (logP=3.09) has higher logP value than paracetamol (logP=0.91).

CONCLUSIONS

Based on the preliminary results obtained, it can be concluded that vegetable oils have the potential to extract pharmaceutically active compounds, especially those with high logP value.

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KEY WORDS

Extraction, vegetable oils, green solvents

POSTER

RAZVOJ I VALIDACIJA HILIC METODE ZA ANALIZU AMLODIPIN-BESILATA I NJEGOVIH NEČISTOĆA

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UVOD I CILJ

Upotrebom hemometrijskog pristupa omogućava se veoma brza procedura u razvoju novih metoda koje se koriste za kontrolu kvaliteta lijekova. U posljednje vrijeme, u analizi lijekova, njihovih nečistoća, zatim metabolita, ali i drugih jedinjenja, veoma su popularne hromatografske metode hidrofilnih interakcija (HILIC). Ova vrsta hromatografije i njihovi retencioni mehanizmi koji obezbjeđuju razdvajanje analiziranih jedinjenja još su potpuno ne razjašnjeni, te predstavljaju i dalje značajno polje istraživanja u svijetu hemije i farmacije. Prvi cilj ovog istraživanja je bio da se upotrebom hemometrijskog pristupa razvije nova HILIC metoda za određivanje amlodipin-besilata i njegovih nečistoća D, E i F. Drugi cilj je bio da se razvije metoda koja će biti ekonomična (imati kratko vrijeme analize – oko 15 minuta). Metoda koja se koristi za analizu ovih analita i koja je opisana u Evropskoj farmakopeji 9.0 traje oko 60 minuta.

METODE

Analize su sprovedene na tečnom hromatografu visokih perfomansi tipa Agilent 1200 (HPLC). Kao stacionarna faza korišćena je HILIC kolona ZORBAX NH2 dimenzija 250 mm x 4,6 mm, 5 µm veličine čestica. Kao metoda optimizacije korišćen je Box-Behnken dizajn, a za ispitivanje robusnosti metode korišćen je frakcioni faktorski dizajn.

REZULTATI

Sprovedenim eksperimentima određeni su optimalni uslovi razdvajanja amlodipin-besilata i njegovih nečistoća D, E i F: sadržaj vodenog rastvora pufera 6% (50 mM amonijum-acetat pH 4,0 podešen sa glacijalnom sirćetnom kiselinom) i sadržaj acetonitrila 94%. Temperatura kolone bila je 30 ° C, detekcija je vršena na 230 nm, brzina protoka mobilne faze 1 mL min^{-1} i zapremina injektovanja 20 µL. Ispitani su i ostali parametri validacije metode (specifičnost, linearnost, tačnost, preciznost i osjetljivost).

ZAKLJUČAK

Hemometrijskim pristupom uspješno je razvijena specifična, tačna, precizna i osjetljiva metoda za analizu amlodipin-besilata i njegovih nečistoća D, E, F u trajanju od 12 minuta.

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KLJUČNE RIJEČI: amlodipin, HILIC, hemometrija

Zahvalnica: Autori ovog rada se zahvaljuju Ministarstvu za naučnotehnološki razvoj, visoko obrazovanje i informaciono društvo koje je istraživanje finansijski podržalo kroz Projekat (19/6-020/961 -73/18).

DEVELOPMENT AND VALIDATION OF A HILIC METHOD FOR ANALYSIS OF AMLODIPINE BESYLATE AND ITS IMPURITIES

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INTRODUCTION

The use of a chemometric approach enables quickly procedure in the development of new methods used to control the quality of drugs. Recently, chromatographic methods of hydrophilic interactions (HILIC) have become very popular in the analysis of drugs, their impurities, their metabolites, as well as other compounds. This type of chromatography and their retention mechanisms that provide separation of the analyzed compounds have not yet been fully elucidated, and remain a significant field of research in the world of chemistry and pharmacy. The first objective of this study was to develop a new HILIC method, by use of chemometric approach, to determine amlodipine besylate and its impurities D, E and F. The second objective was to develop a method that would be economical (short analysis time - about 15 minutes). The method used to analyze these analytes and that is described in European Pharmacopoeia 9.0 takes about 60 minutes.

METHODS

The analyzes were performed on an Agilent 1200 high performance liquid chromatograph (HPLC). As the stationary phase, a HILIC column ZORBAX NH2 dimensions 250 mm x 4.6 mm, 5 µm particle sizes, was used. Box-Behnken design was used as the optimization method, and fractional factor design was used to test the robustness of the method.

RESULTS

The experiments carried out determined the optimum separation conditions of amlodipine besylate and its impurities D, E and F: an aqueous buffer content of 6% (50 mM ammonium acetate pH 4.0 adjusted with glacial acetic acid) and an acetonitrile content of 94%. The column temperature was 30 ° C, the detection was performed at 230 nm, the mobile phase flow rate was 1 mL min^{-1} and the injection volume was 20 µL. Other parameters of the method validation (specificity, linearity, accuracy, precision and sensitivity) were also tested.

CONCLUSION

Specific, accurate, precise and sensitive method for the12 minutes analysis of amlodipine besilate and its impurities D, E, F was successfully developed by chemometric approach.

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KEYWORDS: amlodipine, HILIC, chemometric approach

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POSTER

USPOREDBA SADRŽAJA CINKA U URINU S DVIJE ANALITIČKE METODE

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UVOD I CILJ

Cink je jedan od esencijalnih mikroelemenata vrlo važan za razvoj ljudskog organizma te kao dio mnogih enzima sudjeluje u rastu i razvoju stanica. Na razini organizma je ključan u procesima normalne funkcije imunološkog sustava te male promjene količine mogu dovesti do većeg broja fizioloških poremećaja. Stoga je nužno imati metodu koja omogućava brzo, točno i reproducibilno mjerenje njegove količine. Cilj ovog rada bio je usporediti dvije metode za određivanje cinka u urinu: atomsku apsorpcijsku spektrometriju (AAS) i totalnu rentgensku fluoroscencijsku spektrometriju.

METODE

U svrhu validacije metode na AAS utvrđeni su točnost, preciznost, linearnost, LOD i LOQ [1]. Rezultati dobiveni pomoću TXRF [2] uspoređeni su s rezultatima dobivenim od AAS-a. Za usporedbu rezultata dobivenih dvjema metodama korištena je Bland-Altmanova analiza.

REZULTATI

Provedbom kratke analitičke validacije AAS-a, kao i TXRF, metode za određivanje koncentracije cinka u urinu, pokazalo se da su ispunjeni kriteriji prihvatljivosti za točnost, preciznost, linearnost, LOD i LOQ. Iz dijagrama raspršenja uočeno je da su metode slične za uzorke s nižim koncentracijama cinka, dok je kod uzoraka s višim koncentracija cinka bilo značajnijih odstupanja. Bland-Altmanova analiza pokazala je da, u usporedbi s postojećom metodom određivanja koncentracije cinka u urinu, postoji proporcionalno i konstantno odstupanje između metoda.

ZAKLJUČCI

TXRF tehnika sve se više primjenjuje na širokom spektru uzoraka zbog brže, jednostavnije, multi-elementarne analize u količinama na nivou nanograma kao i niske cijene. Međutim, TXRF metoda pokazala je značajna odstupanja u rezultatima od AAS-a pri višim koncentracijama cinka u uzorku. Stoga je potrebna dodatna analitička optimizacija metode kako bi se TXRF metoda prilagodila uzorcima s visokom koncentracijom cinka.

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[1] Dutra RL, Cantos GA and Carasek E. Analysis of zinc in biological samples by flame atomic absorption spectrometry: use of addition calibration technique. Biol Trace Elem Res 2006, 111(1-3): 265-279.

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KLJUČNE RIJEČI: urin, cink, AAS, TXRF

COMPARISON OF ZINC CONTENT IN URINE WITH TWO ANALYTICAL METHODS

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INTRODUCTION AND OBJECTIVE

Zinc is one of the essential microelements important for the development of human body and participates in the growth and development of cells as part of many enzymes. At the organism level it is crucial for normal function of the immune system and small changes in its amount can lead to a great number of physiological disorders. Therefore, it is necessary to have a method that allows a quick, accurate and reproducible measurement of its quantity. The objective of this work was to compare two methods for zinc determination in urine: Atomic Absorption Spectrometry (AAS) and Total Reflection X-ray Fluorescence Spectrometry (TXRF).

METHODS

For this purpose, accuracy, precision, linearity, LOD and LOQ of AAS method [1] were established. The results obtained by TXRF [2] were compared to those obtained by AAS. Bland-Altman analysis was used to compare the results obtained by two methods.

RESULTS

By carrying out a brief analytical validation of the AAS, as well as the TXRF, method for determining urine zinc concentrations, it has been shown that the eligibility criteria for accuracy, precision, linearity, LOD and LOQ have been met. From the scatterplot, it was observed that the methods were similar at lower concentrations while there were more significant deviations at higher concentrations. Bland-Altman analysis showed that, in comparison with the existing method of zinc concentrations determination in urine there is a proportional and constant deviation between the methods.

CONCLUSIONS

TXRF technique is increasingly applied to a wide spectrum of samples due to faster, simpler, multi-elemental analysis in nanogram quantities at a low cost of maintenance. However, TXRF method had shown significant deviations from AAS at higher concentrations levels. Therefore, additional analytical optimization is needed to adjust TXRF method to samples with high zinc concentration.

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KEY WORDS: urine, cink, AAS, TXRF

POSTER

PRIMJENA NANOČESTICA ZLATA ZA ODREĐIVANJE ANTIOKSIDATIVNOG POTENCIJALA

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UVOD I CILJ

Zbog velikog broja različitih antioksidanasa, promjenljive stabilnosti i načina stvaranja slobodnih radikala, ne postoji univerzalna i validirana metoda za određivanje slobodnih radikala i procjenu antioksidativnog kapaciteta što zahtijeva dizajniranje novih metoda kojima će se preciznije i tačnije određivati antioksidativna aktivnost. U ovom radu izvršen je pregled literature o primjeni nanočestica zlata u antioksidativnim esejima.

METODE

Proučene su i upoređene studije koje se bave ovom tematikom. Tip istraživanja bio je deskriptivni i retrospektivni. Kao izvori informacija korišteni su originalni članci objavljeni u medicinskim časopisima i baze podataka Medline i Google Scholar.

REZULTATI

Glavna karakteristika nanočestica zlata korištena za dizajniranje optičkih eseja je njihova lokalizirana površinska plazmonska rezonanca koja zavisi od geometrije čestica i dielektrične konstante okolnog materijala. Nanočestice osciliraju na frekvenciji unutar vidljivog spektra, emitirajući crvenu boju. Povećanje veličine čestica ili njihova agregacije dovodi do prelaska traka lokalizirane površinske plazmonske rezonance na više talasne dužine, a crvena boja prelazi u plavu. Ova promjena signala direktno je povezana sa količinom antioksidanasa prisutnih u uzorku [1].

Razvijena je modifikovana kolorimetrijska metoda na papiru sa senzorima koji sadrže imobilizirane jone zlata. Antioksidansi reduciraju ove jone, a na površini papira se javlja crvena boja. Ovim se obezbjeđuje jeftina, brza, osjetljiva i robusna analiza [2].

Postoje i metode bazirane na formaciji zlatnih nanoljuski zasnovane na sposobnosti H_2O_2 da reducira jone zlata. Redukcijom nastaju nove ili rastu već postojeće nanočestice zlata u silikatnim jezgrima dok se ne formira kontinuirana ljuska. Antioksidanasi izbacuju H_2O_2 čime se sprječava redukcija zlata i rast nanoljuske. Antioksidativna aktivnost proporcionalna je procentu inhibicije formiranja nanoljuske [3].

ZAKLJUČCI

Metode sa nanočesticama zlata imaju veću osjetljivost, selektivnost i bolje analitičke performanse u poređenju sa konvencionalnim metodama za određivanje antioksidanasa. Međutim, njima se mjeri ukupni sadržaj antioksidanasa tako da ih je potrebno dodatno razvijati kako bi se omogućila kvalitativna i kvantitativna analiza antioksidanasa.

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KLJUČNE RIJEČI: nanočestice zlata, antioksidativni potencijal, nanotehnologija

USAGE OF GOLD NANOPARTICLES IN DETERMINATION OF ANTIOXIDANT POTENTIAL

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INTRODUCTION AND OBJECTIVE

Due to a big number of different antioxidants with variable stability and different ways of producing free radicals, there is no universal nor validated method for the estimation of antioxidant capacity. That requires designing new methods which will be able to determine antioxidant activity more precisely and with more accuracy. This paper shows a literature review of usage gold nanoparticles in antioxidant assays.

METHODS

Studies which concern this subject had been explored and compared. Type of research was descriptive and retrospective. Sources of informations were original articles published in medical journals and databases Medline and Google Scholar.

RESULTS

The main feature of gold nanoparticles used in designing optical assays is their localized surface plasmon resonance which depends on geometry of particles and dielectric constant of surrounding material. Nanoparticles oscillate on frequencies which belong to visible spectrum emitting red light. As particle size increases or as they agregate, the wavelength of surface plasmon resonance shifts to longer and red color becomes blue. This change of signals is directly connected with amount of antioxidants presented in the sample [1].

Modified colorimetric method on paper with sensors and imobilised gold ions is developed. Antioxidants reduce these ions resulting in appearance of red color on the paper surface. This provides cheap, fast, sensitive and robust analysis [2].

There are methods based on formation of gold nanoshells. These methods are based on capacity of H_2O_2 to reduce gold ions. Reduction leads to the creation of new ones or the growth of existing gold nanoparticles in silicate cores until continuous shell is created. The addition of antioxidants leads to ejection of H_2O_2 and that prevents reduction of gold and growth of nanoshell. Antioxidant activity is proportional to the percentage of inhibition of nanoshell formation [3].

CONCLUSIONS

Compared to conventional methods, methods with gold nanoparticles have higher sensitivity, selectivity and analytical performances. However, these methods are used in determination of total content of antioxidants and because of that, they have to be further developed so that they can provide quality and quantity analysis of antioxidants.

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KEY WORDS: gold nanoparticles, antioxidant potential, nanotechnology

POSTER

EVALUACIJA ANTIMIKROBNE I ANTIOKSIDATIVNE AKTIVNOSTI BAKAR(II) I HROM(III) KOMPLEKSA SA SCHIFFOVOM BAZOM IZVEDENOM IZ GLICINA I 2,2-DIHIDROKSIINDAN-1,3-DIONA

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UVOD

Sinteze kompleksa tranzicionih metala sa Schiffovim bazama predstavljaju interesantno područje zbog antimikrobnih, antioksidativnih, antitumorskih i drugih svojstava koji sintetizirani produkti imaju [1-3]. U ovom istraživanju ispitana je antimikrobna i antioksidativna aktivnost produkta interakcije bakar(II) i hrom(III) jona sa Schiffovom bazom izvedenom iz glicina i 2,2-dihidroksiindan-1,3-diona.

METODE

Antimikrobna aktivnost ispitana je difuzionom tehnikom na referentnim sojevima iz ATCC kolekcije. U tu svrhu pripremljeni su rastvori kompleksa koncentracije 5 mg mL^{-1}. Antioksidativna aktivnost ispitana je primjenom FRAP i DPPH metode. Mjerenja su provedena na spektrofotometru Shimadzu UVmini-1240.

REZULTATI

Antimikrobnim screening-om utvrđeno je djelovanje bakar(II) kompleksa protiv *S. aureus* i *C. albicans*, sa zonama inhibicije od 16 i 18 mm. U slučaju hrom(III) kompleksa evidentirano je slabo djelovanje protiv *S. aureus*, sa zonom inhibicije od 11 mm. Antioksidativna aktivnost sintetiziranih kompleksa je visoka sa bliskim IC_{50} vrijednostima od 0,0074 mg mL^{-1} za Cr(III) kompleks i 0,0080 mg mL^{-1} za Cu(II) kompleks. Za koncentracije od 0,04 mg mL^{-1} dobijena je FRAP vrijednost od 238,7 µmol L^{-1} za Cu(II), odnosno 545,5 µmol L^{-1} za Cr(III) kompleks.

ZAKLJUČCI

Iako Cu(II) i Cr(III) kompleksi pokazaju slabo antimikrobno djelovanje, njihov antioksidativni kapacitet je izrazito visok. U poređenju sa publiciranim radovima na istu temu, može se zaključiti da struktura aminokiselina bitno diktira biološku ulogu kompleksa.

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KLJUČNE RIJEČI: kompleksi, DPPH, FRAP, difuzioni metod, UV/Vis

EVALUATION OF ANTIMICROBIAL AND ANTIOXIDANT ACTIVITY OF COPPER (II) AND CHROMIUM (III) COMPLEXES WITH SCHIFF BASE DERIVED FROM GLYCINE AND 2,2-DIHYDROXYINDANE-1,3-DIONE

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INTRODUCTION

Syntheses of the transition metal complexes with Schiff bases represent an interesting field of research due to antimicrobial, antioxidant, antitumor and other properties that the synthesized products have [1-3]. The present study examined the antimicrobial and antioxidant activity of the product of interaction of copper (II) and chromium (III) ions with the Schiff base derived from glycine and 2,2-dihydroxyindane-1,3-dione.

METHODS

Antimicrobial activity was tested by diffusion technique in the reference bacterial strains from the ATCC collection. For this purpose, complex solutions were prepared at 5 mg mL^{-1}. Antioxidant activity was tested using FRAP and DPPH method. Measurements were performed on the Shimadzu UVmini-1240 spectrophotometer.

RESULTS

The antimicrobial screening revealed the effect of copper (II) complex against *S. aureus* and *C. albicans*, with inhibition zones of 16 and 18 mm. In the case of chromium (III) complex, a poor activity was observed against *S. aureus*, with an inhibition zone of 11 mm. The antioxidant activity of the synthesized complexes is high, with IC_{50} values of 0.0074 mg mL^{-1} for the Cr (III) complex and 0.0080 mg mL^{-1} for the Cu (II) complex. For a concentration of 0.04 mg mL^{-1}, FRAP values were obtained in the amount of 238.7 µmol L^{-1} for Cu (II) complex, and 545.5 µmol L^{-1} for Cr (III) complex.

CONCLUSIONS

Although Cu (II) and Cr (III) complexes exhibit poor antimicrobial activity, their antioxidant capacity is extremely high. The structures of amino acids essentially determine the biological role of the complexes, which is in accordance with the results of other published papers on the same topic.

LITERATURE

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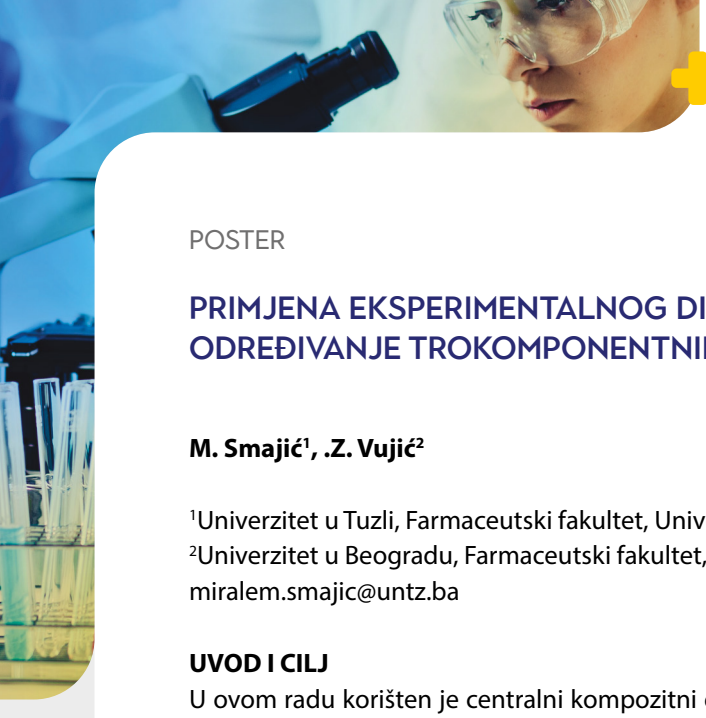
KEY WORDS: complexes, DPPH, FRAP, diffusion method, UV/VIS



POSTER

PRIMJENA EKSPERIMENTALNOG DIZAJNA U OPTIMIZACIJI HPLC METODE ZA ODREĐIVANJE TROKOMPONENTNIH DOZIRNIH OBLIKA

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UVOD I CILJ

U ovom radu korišten je centralni kompozitni eksperimentalni dizajn za brzo, sigurno i precizno određivanje hidrohlorotiazida, amlodipina i valsartana visokoprotočnom tečnom hromatografijom (HPLC) u kombiniranim dozirnim oblicima. Upotrebom ove metode izbjegavaju se nedostaci tradicionalnih analitičkih procedura kao što su dugo vrijeme analize, veliki broj pokušaja, te nemogućnost procjene utjecaja interakcije više faktora na ishod analize.

METODE

Na osnovu preliminarnih eksperimenata i fizičkohemijskih karakteristika analiziranih supstanci, odabrane su tri nezavisne varijable (udio metanola, pH mobilne faze i temperatura kolone) kao ulazni parametri, dok su za izlazne vrijednosti odabrane šest odgovora (retenciono vrijeme hidrohlorotiazida, retenciono vrijeme amlodipina, retenciono vrijeme valsartana, asimetrija hidrohlorotiazida, asimetrija amlodipina i asimetrija valsartana).

REZULTATI

Centralni kompozitni eksperimentalni dizajn omogućava dobijanje podataka o najznačajnijim faktorima koji utiču na izlazne vrijednosti. Nakon optimizacije uslova, separacija je izvršena na koloni Zorbax C_8 (150 mm x 4.6 mm, 5µm) sa mobilnom fazom koja se sastoji od metanola-acetonitrila-acetatnog pufera 40:20:40 (*v/v/v*), pH podešen na 3.5, protokom od 1 mL/min i temperaturi kolone od 40 °C.

ZAKLJUČCI

Razvijena HPLC metoda je uspješno primijenjena na istovremeno razdvajanje aktivnih molekula hidrohlorotiazida, amlodipina i valsartana u njihovim komercijalno dostupnim dozirnim oblicima.

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KLJUČNE RIJEČI: HPLC, centralni kompozitni dizajn, hidrohlorotiazid, amlodipin, valsartan.

APPLICATION OF EXPERIMENTAL DESIGN IN OPTIMIZATION OF HPLC METHOD FOR DETERMINATION OF THREE-COMPONENT DOSAGE FORMS

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INTRODUCTION

Central composite experimental design was used for fast, simple, and accurate high-performance liquid chromatography (HPLC) determination of hydrochlorothiazide, amlodipine and valsartan in combined dosage forms. This method avoids the disadvantages of the traditional analytical approach, which is time-consuming, involves a large number of runs, and does not allow establishing the multiple interacting parameters.

METHOD

On the basis of preliminary experiments and physicochemical characteristic of analyzed substances, three independent variables (methanol content, pH of the mobile phase, and column temperature) were selected as input, while as dependent variables, six responses (retention time of hydrochlorothiazide, retention time of amlodipine, retention time of valsartan, asymmetry of hydrochlorothiazide peak, asymmetry of amlodipine peak, and asymmetry of valsartan peak) were chosen.

RESULTS

Face centered central composite design enables an estimation of investigated factors which have the most importance. After optimizing experimental conditions, a separation was conducted on a Zorbax C8 (150 mm x 4.6 mm, 5µm) column with a mobile phase consisting of methanol-acetonitrile-acetate buffer 40:20:40 (v/v/v), pH adjusted to 3.5 with acetic acid, flow rate of 1 mL/min and column temperature was set at 40 °C.

CONCLUSION

The developed HPLC method was successfully applied to the simultaneous separations of these active drug compounds in their commercial dosage forms.

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KEY WORDS: HPLC, centrale composite design dizajn, hydrochlorotiazid, amlodipine, valsartane.

POSTER

AMPEROMETRIJSKO ISPITIVANJE UTICAJA PH VRIJEDNOSTI MOBILNE FAZE NA ELEKTROHEMIJSKU OKSIDACIJU ORGANOSUMPORNIH SPOJEVA

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UVOD I CILJ

Amperometrija je elektrohemijska metoda koja ima određene prednosti u odnosu na druge metode koje se koriste za kvantifikaciju organosumpornih spojeva [1]. Spojevi koji u svom sastavu sadrže sumpor važne su molekule kako u okruženju, tako i u biološkim procesima, indikatori su velikog broja oboljenja i aktivne komponente u farmaceutskim preparatima. Važan parametar za amperometrijska mjerenja je pH vrijednost mobilne faze, koja utiče u velikoj mjeri na elektrohemijsku oksidaciju ispitivanog analita na elektrodi i strujni odziv. Cilj ovog istraživanja je amperometrijskom metodom ispitati uticaj pH vrijednosti mobilne faze na elektrohemijsku oksidaciju i strujni odziv organosumpornih spojeva na ugljikovoj elektrodi koja je modificirana ugljikovim nanocjevčicama sa više zidova (MWCNTs).

METODE

Uticaj pH vrijednosti mobilne faze na elektrohemijsku oksidaciju ispitan je za šest organosumpornih spojeva: *L*-cistein ($C_3H_7NO_2S$), 2,5-dimerkapto-1,3,4-tiodiazol ($C_2H_2N_2S_3$), glutation reducirani ($C_{10}H_{17}N_3O_6S$), natrij dimetilditiokarbamat ($C_3H_6NNaS_2$), tio semikarbazid (CH_5N_3S) i tioureu ($CS(NH_2)_2$). Analiza je urađena pomoću protočno-injekcione amperometrije (FIA) upotrebom elektrode od staklastog ugljika modificirane sa MWCNTs. Kao mobilna faza korišten je fosfatni pufer (NaH_2PO_4 / Na_2HPO_4, 0.10 mol/L) pH vrijednosti od 3 do 9.

REZULTATI

Podaci dobiveni amperometrijskim mjerenjima pokazali su da je elektrokatalitički odgovor prisutan u rasponu pH vrijednosti od 3 do 9. Svi organosumporni spojevi daju nagli porast strujnog odziva u baznoj sredini. Od analiziranih spojeva najveće vrijednosti strujnog odziva zabilježene su za $C_3H_7NO_2S$, a najmanje za $C_{10}H_{17}N_3O_6S$.

ZAKLJUČCI

Na osnovu dobivenih rezultata može se zaključiti da organosumporni spojevi daju stabilan struni odziv u širokom rasponu pH vrijednosti mobilne faze. U kiseloj sredini otežana je deprotonizacija tiolne grupe, a samim tim i redoks proces [2]. Strujni odziv, za sve oranosumporne spojeve, ima manje vrijednosti u kiseloj sredini u odnosu na neutralnu i baznu sredinu.

LITERATURA

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KLJUČNE RIJEČI: amperometrija, pH, organosumporni spojevi, mobilna faza.

AMPEROMETRIC INVESTIGATION THE INFLUENCE OF PH VALUE OF THE MOBILE PHASE ON THE ELECTROCHEMICAL OXIDATION OF ORGANOSULFUR COMPOUNDS

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INTRODUCTION AND OBJECTIVE

Amperometry is an electrochemical method which takes some advantage compared to other methods used for the quantification of organosulfur compounds [1]. Sulfur-containing compounds are important molecules in the environment and biological processes. Furthermore, they are indicators of a large number of diseases and active components in pharmaceutical preparations. An important parameter for the amperometric measurement is the pH of the mobile phase, which significantly affects the electrochemical oxidation of the examined analyte at the electrode and the current response. The aim of the present study is to investigate, by amperometric method, the effect of pH value of the mobile phase on the electrochemical oxidation and current response of organosulfur compounds on carbon electrode modified with multi-wall carbon nanotubes (MWCNTs).

METHODS

The influence of pH value of the mobile phase on the electrochemical oxidation was examined for six organosulfur compounds: *L*- cysteine ($C_3H_7NO_2S$), 2,5-dimercapto-1,3,4-thiadiazole ($C_2H_2N_2S_3$), glutathione reduced ($C_{10}H_{17}N_3O_6S$), sodium dimethyldithiocarbamate ($C_3H_6NNaS_2$), thiosemicarbazide (CH_5N_3S) and thiourea ($CS(NH_2)_2$). The analysis was performed by flow injection amperometry (FIA) using a glassy carbon electrode modified with MWCNTs. Phosphate buffer (NaH_2PO_4 / Na_2HPO_4, 0.10 mol/L) was used as the mobile phase whose pH was from 3 to 9.

RESULTS

The data obtained by amperometric measurements indicated that the electrocatalytic response is present in the pH range from 3 to 9. All organosulfur compounds give a swift increase in the current response in the alkaline medium. Organosulfur compound $C_3H_7NO_2S$ gave the highest values of current response and $C_{10}H_{17}N_3O_6S$ at least.

CONCLUSIONS

Based on the obtained results, it can be concluded that organosulfur compounds give a stable current response over a wide range of pH values of the mobile phase. In the acidic medium, deprotonation of the thiol group is difficult, and therefore the redox process [2]. The current response, for all organosulfur compounds, has lower values in the acidic medium compared to the neutral and basic.

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KEY WORDS: amperometry, pH, oranosulfur compounds, mobile phase.

POSTER

DFT STUDIJA N-3 SUPSTITUIRANIH DERIVATA PIRIMIDINA

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UVOD I CILJ

Funkcionalna teorija gustoće (eng. *density functional theory*, DFT) je kompjuterska kvantno-hemijska metoda koja se koristi u istraživanju elektronske strukture atoma, molekula i kondenziranih faza, s ciljem molekulskog modeliranja. Pomoću ove teorije svojstva mnogih sistema mogu se odrediti koristeći funkcije drugih funkcija tj. funkcionale, koji su zapravo elektronska gustoća. Nukleozidni analozi mogu biti derivati pirimidina i purina, sa različitim mehanizmom djelovanja. Najznačajniji antiviralni lijekovi su dobiveni strukturnim modifikacijama prirodnih nukleozida u položaju C5, ili primarne alkoholne grupe dezoksiriboze, odnosno riboze [1,2]. Stoga je glavni cilj ovog rada da se analiziraju novosintetizirani *N*-3 derivati pirimidina [3] pomoću kvantno-hemijske metode (DFT).

METODA

Svi proračuni su izvedeni na B3LYP/6-31G* teorijskom nivou, pomoću programa Spartan 14. Izračunati su: elektronski hemijski potencijal, razlika u HOMO/LUMO energiji, dipolni moment, vibraciona frekvencija, elektrofilnost, hemijska tvrdoća i logP.

REZULTATI

Dobiveni podaci hemijskih reakcionih deskriptora su poslužili za predviđanje stabilnosti i reaktivnosti *N*-3 supstituiranih derivata pirimidina. Također, dobiveni rezultati su se poredili sa eksperimentalnim podacima i sa nekim farmakološkim osobinama analiziranih spojeva. Antimikrobna aktivnost *N*-3 supstituiranih derivata pirimidina određena je na sojevima: *Bacillus subtilis* ATCC 6633, *Bacillus cereus* ATCC 11778, *Staphylococcus aureus* ATCC 6538P, *Staphylococcus epidermidis* ATCC 12228, *Echerichia coli* ATCC 8739, *Candida albicans* ATCC 10231, *Sacharomices cerevisie* ATCC 9763, *Pseudomonas aeruginosa* ATCC 9027 metodom dilucije.

ZAKLJUČCI

Teorijska karakterizacija odgovara eksperimentalnim podacima i dobivena je dobra korelacija. Dobivene vrijednosti minimalne inhibitorne koncentracije (MIC) se dobro slažu sa izračunatim deskriptorima hemijske reaktivnosti.

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KLJUČNE RIJEČI: DFT, *N*-3 supstituirani derivati pirimidina.

DFT STUDY OF N-3 SUBSTITUTED DERIVATIVES OF PYRIMIDINE

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INTRODUCTION AND OBJECTIVE

Functional density theory (DFT) is a computational quantum chemical method used to investigate the electron structures of atoms, molecules, and condensed phases, using a molecular model. Propertys many of systems can be were determine by this theory used the functions of other functions, which are actually the electron density. Nucleoside analogs can be pyrimidine and purine derivatives, with different mechanisms of activity. The most important antiviral drugs were obtained by structural modifications of the natural nucleosides in the C5 region, or the primary alcoholic group of deoxyribose, or ribose [1,2]. Therefore, the aim of this study was to analyze newly synthesized *N*-3 pyrimidine derivatives [3] using the quantum-chemical method (DFT).

METHOD

All calculations were performed at B3LYP / 6-31G* theoretical level, using Spartan 14.

Calculated were: electron chemical potential, the difference in HOMO / LUMO energy, dipole moment, vibrational frequency, electrophilicity, chemical hardness and logP.

RESULTS

The obtained data of chemical reaction descriptor were used to predict the stability and reactivity of *N*-3 substituted derivatives of pyrimidine. Also, the obtained results were compared with experimental data and with some pharmacological properties of the analyzed compounds. The antimicrobial activity of the *N*-3 substituted derivatives of pyrimidine was determined on the standard strains: *Bacillus subtilis* ATCC 6633, *Bacillus cereus* ATCC 11778, *Staphylococcus aureus* ATCC 6538P, *Staphylococcus epidermidis* ATCC 12228, *Echerichia coli* ATCC 8739, *Candida albicans* ATCC 10231, *Sacharomices cerevisie* ATCC 9763, *Pseudomonas aeruginosa* ATCC 9027 by dilution method.

CONCLUSIONS

Theoretical characterization is coincidence with the experimental data and a good correlation was achieved. The obtained values of minimum inhibitory concentration (MIC) agree well with chemical reactivity descriptors of the molecules.

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[3] Osmanović A., Salihović M., Kopjar N., Želježić D., Roca S., Špirtović-Halilović S., Šapčanin A., Završnik D. Synthesis of New Acyclic Pyrimidine Nucleoside Analogues and Preliminary Assessment of Their Cytotoxic and Genotoxic Effects In Vitro. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*. 2019;10(1):493-502.

KEYWORDS: DFT, *N*-3 pyrimidine derivatives.

POSTER

ODNOS STRUKTURE I AKTIVNOSTI TESTOSTERONA

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UVOD I CILJ

Testosteron je najvažniji androgeni hormon .(koji se kod muškaraca produkuje u testisima) (Testosteron je odgovoran za) anaboličke (izgradnja mišića) i androgene (razvijanje muških sekundarnih spolnih karakteristika) efekte. Proučavanje odnosa strukture i farmakološke aktivnosti anaboličkih steroida otvara mogućnost izmjene ponašanja tih supstanci u organizmu, ali i pojačavanja njihovih efekata.

METODE

U ovom radu urađen je pregled radova koji proučavaju odnos strukture i aktivnosti anaboličkih steroida.

REZULTATI

Cilj strukturne modifikacije molekule testosterona je dobijanje lijekova sa poboljšanom farmakokinetikom kako bi se olakšala terapija starosno-zavisne androgene insuficijencije. Osim toga, moguće je modificirati testosteron i smanjiti njegove androgene, a pojačati anaboličke efekte pri čemu se dobijaju agensi koji poboljšavaju sportske performanse, ali ne uzrokuju neželjene efekate, zbog kojih je većina steroida zabranjena za upotrebu u sportu.

ZAKLJUČCI

Trenutno su u istraživanju novi lijekovi sa velikim potencijalom u ovoj oblasti, jer pokazuju korisne efekte bez neželjenih efekata povezanih sa anaboličkim steroidima, te bi mogli potisnuti iz upotrebe postojeće anaboličke steroide.

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KLJUČNE RIJEČI: odnos strukture i farmakološke aktivnosti, anabolički steroidi, testosteron

STRUCTURE-ACTIVITY RELATIONSHIP OF TESTOSTERON

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INTRODUCTION

Testosterone is main androgen hormone and is secreted by testicles in males. It produces anabolic (build muscles) and androgen (develop male secondary sex characteristics) effects. Studying the structure-activity relationship of anabolic steroids opens up possibilities to alter the behavior of these substances in organism as well as to boost their potency.

METHOD

This paper provides an overview of the scientific work that has examined the structure and activity relationship of anabolic steroids.

RESULTS

The goal of modification of testosterone molecule is to get drugs with enhanced pharmacokinetic so that treatement of aging-related androgen insufficiency becomes easier. Also, it is possible to modificate testosterone to reduce its androgen effects and boost anabolic ones in order to get agents which enhance sport's performances, but they have harmful effects as well and many of them are banned.

CONCLUSION

Currently, new drugs are developing that have big potential in this area since they show useful effects without unwanted side effects related to anabolic steroids, and they can render anabolic steroids obsolete.

KEY WORDS: structure-activity relationship, anabolic steroids, testosterone

POSTER

ISPITIVANJE MIKROBIOLOŠKOG I FIZIČKO-HEMIJSKOG KVALITETA DESTILOVANE VODE

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UVOD I CILJ

Destilovana voda predstavlja najčešće korištenu sirovinu u farmaceutskoj industriji. Prilikom izrade farmaceutskih preparata najčešće ima ulogu rastvarača, vehikuluma, diluensa i adjuvensa. Zbog široke upotrebe treba zadovoljavati fizičko-hemijske i mikrobiološke parametre propisane Evropskom farmakopejom. Cilj ovog rada bio je ispitati mikrobiološki i fizičko-hemijski kvalitet destilovane vode koja se koristi u apotekama u Bosni i Hercegovini [1,2].

METODE

Analizirano je 10 uzoraka destilovane vode od pet različitih proizvođača, iz različitih apoteka širom BiH. Uzorci su fitrirani kroz membranski filter veličine pora 0,45 µm. Filter papir je zasijan na hranjivoj podlozi i inkubiran na 30-35˚C minimalno 5 dana. Uzorci su sakupljani u 5 vremenskih intervala (0, 5, 10, 15, i 30 dana nakon otvaranja) i testirani na prisustvo *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus*, koliformnih bakterija, te je određen ukupan broj živih bakterija. Fizičko-hemijski kvalitet je ispitan prema zahtjevima Evropske farmakopeje [2].

REZULTATI

Od 10 ispitivanih uzoraka, samo je jedan bio mikrobiološki ispravan (manji broj živih bakterija od dozvoljenog). Svi ostali uzorci su imali broj živih bakterija znatno veći od dozvoljenog. Niti u jednom uzorku nije dokazano prisustvo *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus* i koliformnih bakterija. Rezultati ispitivanja fizičko-hemijskog kvaliteta pokazali su da dva uzorka imaju provodljivost veću od dozvoljene, tri uzorka imaju prekoračen limit za teške metale, a kod dva uzorka je dokazano prisustvo oksidujućih supstanci.

ZAKLJUČCI

Na osnovu sprovedene preliminarne studije može se pretpostaviti da se u apotekama širom BiH koristi destilovana voda koja ne zadovoljava u potpunosti fizičko-hemijske i mikrobiološke kriterijume propisane Evropskom farmakopejom. Neadekvatna destilovana voda može ugroziti stabilnost farmaceutskog preparata, kao i bezbjednost pacijenta. S obzirom da se u apotekama ova voda često koristi u pedijatrijskoj populaciji za rekonstituciju antibiotskih praškova, od velikog je značaja da u potpunosti zadovoljava zahtjeve kvaliteta.

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KLJUČNE RIJEČI: destilovana voda, fizičko-hemijski i mikrobiološki kvalitet, praškovi za oralne suspenzije

Zahvalnica: *Autori se zahvaljuju Ministarstvu za naučnotehnološki razvoj, visoko obrazovanje i informaciono društvo Republike Srpske, na podršci prilikom sprovođenja ovog istraživanja u sklopu Projekta (19/6-020/961-73/18).*

MICROBIOLOGICAL AND PHYSICOCHEMICAL QUALITY TESTING OF DISTILLED WATER

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INTRODUCTION

Distilled water is one of the most frequently used resources in pharmaceutical industry. In the production of pharmaceutical preparations, it is widely used as a solvent, vehiculum, diluent and adjuvant. Due to its wide use, physicochemical and microbiological parameters prescribed by the European Pharmacopoeia, should be satisfied. The aim of this paper was to examine physicochemical and microbiological quality of distilled water used in pharmacies in Bosnia and Herzegovina [1,2].

METHODS

We analyzed 10 samples of distilled water from five different manufacturers, bought in different pharmacies in BiH. Samples were filtrated through a membrane filter (pore size 0.45 μm). Filter paper was seeded on the nutrient medium and incubated at 30-35 °C for a minimum of 5 days. Samples were taken in five time intervals (0, 5, 10, 15 and 30 days after opening) and tested for the presence of *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus* and coliform bacteria, and number of alive bacteria was also investigated. Physicochemical quality was tested according to requirements of European Pharmacopoeia.

RESULTS

Only one sample met the criteria for microbiological quality prescribed by the pharmacopoeia. All other samples had higher number of alive bacteria than allowed. Presence of *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus* and coliform bacteria, wasn't proven. Results showed that 2 samples had conductivity greater than permissible, 3 samples exceeded the limit for heavy metals, and 2 samples showed presence of oxidisable substances.

CONCLUSIONS

Based on this preliminary study, it can be assumed that distilled water in pharmacies across BiH, does not fully meet physicochemical and microbiological criteria prescribed by the European Pharmacopoeia. Inadequate distilled water could endanger stability of the pharmaceutical preparation and safety of patients. Considering that in pharmacies this water is often used in pediatric population for the reconstitution of antibiotic powders, it is of great importance that it fully meets quality requirements.

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KEY WORDS: distilled water, physicochemical and microbiological quality, powders for oral suspensions

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POSTER

KOMPLEKSOMETRIJSKO ODREĐIVANJE SADRŽAJA MAGNEZIJA U FARMACEUTSKIM PREPARATIMA

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UVOD I CILJ

Magnezij je esencijalni element i intraćelijski dvovalentni katjon uključen u više od 300 biohemijskih funkcija (1). Moderan način života utiče da većina osoba imaju nedostatak magnezija i za normalno funkcionisanje organizma moraju ga unositi dodatno u formi različitih suplemenata. Magnezijum oksid (MgO) je najčešća forma suplementa magnezijuma koja je dostupna u apotekama (2). U ovom radu, određen je sadržaj magnezijuma u tri farmaceutska preparata, različitih proizvođača prisutnih na tržištu u Kantonu Sarajevo.

METODE

Odabrani suplementi za analizu imali su deklarisani sadržaj magnezijuma u formi MgO od 300, 400, i 375 mg MgO. Otopine uzoraka preparata pripremljene su u tri paralelke, otapanjem sadržaja tableta u hloridnoj kiselini i kompleksometrijskim određivanjem sadržaja magnezija standardnom otopinom etilendiaminotetrasirćetne kiseline (EDTA) (3).

REZULTATI

Komleksometrijsko određivanje temeljeno na reakciji između magnezijum jona i otopine EDTA pokazao je sadržaj Mg od 311, 399, i 385 mg iz MgO, respektivno prema deklarisanom sadržaju na pakovanju od strane proizvođača na nasumično odabranim suplementima.

ZAKLJUČCI

Svi analizirani komercijalno dostupni suplementi magnezija u obliku MgO pokazali su nivoe magnezijuma koje mogu zadovoljiti dnevno preporučene vrijednosti za odrasle u rasponu od 300 do 400 mg.

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KLJUČNE RIJEČI: magnezij, suplementacija, kompleksometrija

COMPLEXOMETRIC DETERMINATION OF MAGNESIUM CONTENT IN PHARMACEUTICAL PREPARATIONS

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INTRODUCTION AND OBJECTIVE

Magnesium is an essential element and an intracellular divalent cation which is involved in more than 300 biochemical functions (1). Modern lifestyle affects that most of people have deficiency of magnesium and for normal functioning of the organism they must intake it additionally in the form of different supplements. Magnesium oxide is the most common form of magnesium supplement available in pharmacies (2). In this work, magnesium content was determined in three pharmaceutical preparations, and different producers present in the market in Canton Sarajevo.

METHODS

The selected supplements for the analysis had the declared magnesium content in the form of MgO of 300mg, 400mg, and 375 mg of Mg, respectively. The sample solutions were prepared in three parallels, by dissolving the contents of the tablets in hydrochloric acid and by complexometric determination of the magnesium content by standard ethylenediaminetetraacetic acid (EDTA) solution (3).

RESULTS

The complexometric determination based on the reaction between the magnesium ions and the EDTA solution showed the content of Mg were 311mg, 399mg and 385 mg of MgO, respectively according to the declared content on packaging by the manufacturer on randomly selected supplements.

CONCLUSIONS

All tested commercially available magnesium supplements in the form of MgO showed levels of magnesium that can supply daily Mg recommended values for adults ranging from 300 to 400 mg.

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KEYWORDS: magnesium, supplementation, complexometry

POSTER

FITOSINTEZA TiO_2 NANOČESTICA ZA BIOMEDICINSKE SVRHE: ANTIMIKROBNI I FARMAKODINAMIČKI ASPEKT

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UVOD I CILJ

Biomedicinska primjena TiO_2 nanočestica (TiO_2NPs) se zasniva na veličini TiO_2 nanočestica, morfologiji i stabilnosti. Poželjne karakteristike TiO_2 nanočestica kao što su biokompatibilnost i minimalna agregacija se mogu očuvati upotrebom postupka zelene hemije. Postupak zelene hemije ima prednost nad hemijskim načinom sinteze jer je jeftiniji i ekološki prihvatljiv. Fitosintetisane TiO_2 nanočestice su podvrgnute mikrobiološkoj analizi i *in vitro time – kill* pristupu. Detaljnije informacije o antimikrobnoj aktivnosti fitosintetisanih nanočestica titanijum dioksida mogu se dobiti pomoću *in vitro time - kill* eksperimenata. Dobijene *time-kill* krive mogu poslužiti za konstruisanje farmakodinamičkog matematičkog modela sa ciljem opisivanja vremenskog toka antimikrobnog dejstva, izračunavanja odgovarajućih farmakodinamičkih parametara i ispitivanja uticaja karakteristika fitosintetisanih nanočestica na antimikrobno dejstvo.

EKSPERIMENTALNE METODE:

U istraživanju TiO_2 nanočestice su sintetisane primjenom hemijskog postupka i postupka zelene hemije uz korištenje ekstrakta cvijeta hibiskusa Za karakterizaciju TiO_2 NPs korišteni su sledeći instrumenti: FT-IR (Tensor 27 instrument), UV/VIS spektrofotometar (Shimadzu UV-1900) i termalne tehnike (TA SDT 2060 uređaj za simultanu TGA/DTA analizu). Antimikrobni test je urađen difuznom metodom na Muller-Hinton substratu za izolate Acinetobacter baumannii, methicillin resistant Staphylococcus aureus (MRSA), methicillin sensitive S. a (MSMA), Escherichia coli i Pseudomonas aeruginosa. Protokol za farmakodinamičku analizu preko *in vitro time – kill* pristupa je postavljen.

REZULTATI:

Prisustvo TiO_2 nanočestica je potvrđeno primjenom UV/VIS spektrofotometrije sa pikom na 423 nm. Dodatne potvrdne analize su urađene sa FT-IR spektrima. TGA/DTA metoda je potvrdila prisustvo dvije polimorfne forme anatasa i rutila i pokazala je da je termička stabilnost uzoraka sintetisanih metodom zelene hemije značajno umanjena i da ti uzorci brže podliježu termičkoj dekompoziciji. TiO_2 nanočestice sintetisane pomoću oba metoda pokazale su dobru antimikrobnu aktivnost. Njihova antimikrobna aktivnost je rezultat njihove interakcije sa ćelijom bakterije, vjerovatno zbog fotokatalitičke aktivnosti TiO_2 NPs. Na osnovu ovih podataka razmatran je protokol za farmakodinamički model.

ZAKLJUČCI:

Istraživanje je pokazalo da TiO_2 NPs nanočestice sintetisane metodom precipitacije i zelene hemije imaju antimikrobnu aktivnost i mogu se koristiti kao antibakterijski agensi.

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KLJUČNE RIJEČI: titanijum oksid, fitosinteza, antimikrobni efekat, time-kill krive

Zahvalnica: *Autori se zahvaljuju Ministarstvu za naučni i tehnološki razvoj, visoko obrazovanje i informaciono društvo Republike Srpske kroz projekta 19/6-020/961-74/18.*

PHYTOSYNTHESIS OF TiO_2 NANOPARTICLES FOR BIOMEDICAL USES: ANTIMICROBIAL AND PHARMACODYNAMIC ASSPECT

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INTRODUCTION:
Biomedical application of TiO_2 nanoparticles (TiO_2NPs) is dependent on TiO_2 particles dimension, morphology and stability of synthesized nanoparticles. Desirable characteristics of good TiO_2 nanoparticles such as biocompatibility and minimal aggregation are well maintained by the green chemistry synthesis methods. Green synthesis provides advantages over chemical methods because it is not only cost effective but also environment-friendly. Phytosyntesized TiO_2 nanoparticles were subjected to microbiology and *in vitro time – kill* approach. Time-kill curves can provide a sufficient information for construction of pharmacodynamic mathematical model which serves as good base for description of the antimicrobial effect time course, calculation of appropriate pharmacodynamic parameters, as well as impact of phytosynthesized TiO_2 nanoparticle characteristics on antimicrobial activity.

EXPERIMENTAL METHODS:
TiO_2 nanoparticles were synthesized using chemical precipitation and green chemistry method in which hibiscus flower extract was used. For characterisation of TiO_2 NPs following instruments were used: FT-IR (Tensor 27 instrument), UV/VIS spectrophotometry (Shimadzu UV-1900) and thermal methods (TA SDT 2060 device for simultaneous TGA/DTA analysis). Antimicrobial activity was tested by diffusion method on a Muller-Hinton agara for Acinetobacter baumannii, methicillin resistant Staphylococcus aureus (MRSA), methicillin sensitive S. a (MSMA), Escherichia coli and Pseudomonas aeruginosa. Protocol for pharmacodynamic analysis via *in vitro time – kill* approach was determined.

RESULTS:
Presence of TiO_2 nanoparticles was confirmed using UV/VIS spectrophotometry with peak present at 423 nm. Additionaly FT-IR spectra also confirmed the presence of TiO_2 NPs. TGA revealed existance of two polymorphic anatase-rutile formations and one very interesting feature which showed that TiO_2 NPs obtained by green chemistry method have significantly lower thermal stability and therefore thermaly decompose before chemically obtained TiO_2. TiO_2 NPs synthesized by both methods showed good antimicrobial activity. TiO_2 NPs antimicrobial activity is attributed to their interaction with the bacteria cell, probably due to photocatalytical activity of TiO_2 NPs. Based on obtained results protocol for pharmacodynamic model was evaluated.

CONCLUSIONS:
Based on this study, TiO_2 NPs synthesized by precipitation method and green chemistry method have antibacterial effect and can be used as an antibacterial agent for different purposes.

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KEY WORDS: titanium oxide, phytosynthesis, antimicrobial effect, time-kill curves

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SPONZORISANA PREDAVANJA

SATELITSKI SIMPOZIJ HEMOFARM

SAVREMENI ASPEKTI PRIMJENE PROBIOTIKA

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Disbiozom se naziva promena u sastavu crevne mikrobiote koja može biti osnova za nastanak mnogih oboljenja kako digestivnog trakta tako i organizma uopšte. Na promenu mikrobiote mogu da utiču stres, upotreba lekova, godine starosti. Jedan od mogućih načina obnavljanja nastalog poremećaja i ponovno uspostavljanja balansa u sastavu, broju i raznolikosti mikroorganizama u digestivnom traktu je i upotreba probiotika. Probiotici su živi mikroorganizmi koji, kada se unesu u dovoljnim količinama, mogu imati blagotvorno dejstvo na ljudsko zdravlje. U poslednje dve decenije, poraslo je interesovanje širom sveta za korišćenje najpre namirnica koje sadrže probiotske bakterijske kulture ali i samih probiotskih sojeva kao dodatka ishrani, pomoćnih medicinskih sredstava pa čak i kao lekova. Svakim se danom otkrivaju nove moguće indikacije za upotrebu specifičnih probiotskih sojeva. Među najznačajnijim izdvaja se prevencija dijareje udružene sa upotrebom antibiotika, prevencija kolitisa udruženog sa Clostridium difficile infekcijom, zatim eradikacija Helicobacter pylori infekcije, ali i druga oboljenja kod kojih upotreba probiotika može biti od koristi kao što su sindrom nervoznog creva, masna jetra, preterana telesna masa, ulcerozni kolitis i dr. Povećana upotreba probiotika nameće i potrebu za praćenjem efekta njihovog korišćenja, pogotovu što se radi o živim mikroorganizmima. Osnovni principi kvaliteta probiotika podrazumevaju soj, specifičnost soja, proces proizvodnje, bezbednost, preporuke za njihovu upotrebu. Cilj kontinuirane edukacije je upoznati slušaoce sa dostupnim podacima o indikacijama, pravilnoj upotrebi i sigurnosti probiotika za ljudsku upotrebu u svakodnevnoj kliničkoj praksi

SPONZORISANA PREDAVANJA

SALVEO

PSIHOLOGIJA I MARKETING U DIGITALNO DOBA

Dalibor Šumiga

Uz porast popularnosti interneta pojavio se i trend samodijagnoze uz pomoć dr. Google, širenja neprovjerenih informacija o zdravlju i manjka ljudskog kontakta.

Je li digitalno doba zapravo mračno doba našeg društva? Je li nekad bilo bolje i gdje je u svemu tome farmaceutska industrija?

Specijalist za bihevioralni marketing, Dalibor Šumiga, u svojem izlaganju pokazat će rezultate bihevioralnih istraživanja koja bacaju malo drugačije svjetlo na većinu onoga što trenutno znamo i čitamo.

SPONZORISANA PREDAVANJA

SATELITSKI SIMPOZIJ VICHY

NORMADERM PHYTOSOLUTION – NOVA FORMULA U LIJEČENJU ACNE

Prof. dr. Dubravka Šimić

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Acne je kronična upalna bolest pilosebacealnog aparata uzrokovana brojnim čimbenicima. Temeljna promjena je mikrokomedon nastao kao posljedica poremećene produkcije loja, abnormalne diferencijacije keratinocita i imunog odgovora na upalu uzrokovanu kolonizacijom *Propionibacterium acnes*. Iz mikrokomedona nastaju promjene vidljive u kliničkoj slici *acne*: komedon (crni i bijeli), papula, pustula i nodus, a nove spoznaje dokazuju važnu ulogu nespecifičnog imunog odgovora u pobrojanim lezijama. Stoga stimulacija produkcije proupalnih medijatora dovode do drugačijeg pristupa u liječenju *acne*. Samostalno liječenje, bilo ono lokalno ili opće, često je neučinkovito. Čimbenici ekspozoma uključuju prehranu, klimatske faktore, upotrebu lijekova, zagađenje, zanimanje, psihosocijalne faktore i životni i mogu utjecati na razvoj i kliničku sliku akne kao i na učinkovitost tretmana Slabljenjem barijerne funkcije koža postaje fragilnija pa težina kliničke slike akne korelira sa stupnjom izmjene barijerne funkcije kože.

Nova formula iz Vichy-a u liječenju *acne* je *Normaderm Phytosolution.* Sadržava 60% Vichy termalne vode, 2% prirodne salicilne kisleine (dobijena destilacijom i hidrolizom iz biljke *gaulterija*), šećer fikosaharid dobijen iz alge *Laminaria digitata* koji ima svojstvo inhibicije akumulacije lipida u humanim sebocitima koji uzrokuju hiperseboreju. Vitamin Cg u formuli je u koncentraciji 0,2%, derivat je vitamina C poznat kao antioksidans i blokator sinteze melanina pa osigurava antiinflamatorni i depigmentacijski učinak. Formula uključuje i 0,2% hijaluronske kiseline prirodnog porijekla. Ovaj polisaharid dobijen je procesom fermentacije iz pšenice, poznat je po svojim higroskopskih osobinama (vezuje veliku količinu vode) i stvara i zaštitni film na površini kože. Tekstura *Normaderm Phytosolutiona* je opalescentni gel serum, brzo se upija u kožu, dobro hidrira kožu ali je ostvaljva matiranom i bez tragova kreme. Ima blagi miris baziran na notama zelenog čaja. Kombinirajući kliničku učinkovitost i izvrsnu kozmetičnost *Normaderm Phytosolution* je saveznik u preuzimanju kontrole kože ove kronične upalne bolesti.

NORMADERM PHYTOSOLUTION - A NEW FORMULA IN ACNE TREATMENT

Prof. dr. Dubravka Šimić

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Acne is a chronic inflammatory disease of the pilosebaceous apparatus caused by a number of factors. The fundamental change is the microcomedone resulting from impaired tallow production, abnormal differentiation of keratinocytes, and the immune response to inflammation caused by the colonization of Propionibacterium acnes. Microcomedons produce changes visible in the clinical picture of acne: comedone (black and white), papules, pustules, and nodules, and new insights prove the important role of the nonspecific immune response in the listed lesions. Therefore, stimulating the production of proinflammatory mediators leads to a different approach in the treatment of acne. Self-medication, whether local or general, is often ineffective. Exposure factors include diet, climatic factors, medication use, pollution, occupation, psychosocial factors, and lifestyle, and can affect the development and clinical picture of acne as well as the effectiveness of treatment skin. By weakening the barrier function, the skin becomes more fragile, so the severity of the clinical picture of acne correlates with the degree of alteration of the skin barrier function.

The new Vichy formula for acne treatment is *Normaderm Phytosolution*. Contains 60% Vichy thermal water, 2% natural salicylic acid (obtained by distillation and hydrolysis from a *gaulteria plant*), a phycosaccharide sugar obtained from the *Laminaria digitata algae*, which has the ability to inhibit the accumulation of lipids in human sebocytes causing hyperseborea. Vitamin Cg in the formula is at a concentration of 0.2%, a derivative of vitamin C known as an antioxidant and blocker of melanin synthesis, thus providing an anti-inflammatory and depigmentation effect. The formula also includes 0.2% hyaluronic acid of natural origin. This polysaccharide is obtained by the fermentation process from wheat, is known for its hygroscopic properties (binds large amounts of water) and also forms a protective film on the surface of the skin. Normaderm Phytosolution's texture is an opalescent gel serum, absorbs quickly into the skin, moisturizes the skin well but leaves it matte and without any trace of cream. It has a slight aroma based on notes of green tea. Combining clinical efficacy and excellent cosmetics, Normaderm Phytosolution is an ally in taking control of the skin of this chronic inflammatory disease.

SATELITSKI SIMPOZIJ ABELA PHARM

ZNAČAJ STABILNOSTI PROBIOTSKIH PREPARATA ZA NJIHOVU BEZBEDNOST I EFIKASNOST

Davor J. Korčok, Nada Tršić-Milanović, Bogdan Mitić

Abela Pharm d.o.o., Viline vode b.b., 11000 Beograd, Srbija

SVRHA RADA:
Probiotici su proizvodi definisani kao: živi mikroorganizmi koji kada se primenjuju u odgovarajućim količinama deluju povoljno na zdravlje domaćina, i u prometu mogu pronaći kao farmaceutsko- dozirani oblici registrovani kao: lekovi, dijetetski suplementi i kao medicinska sredstva. Glavni cilj ovog rada bio je adekvatno postavljanje faza pri proizvodnji probiotika u cilju dobijanja kvalitetnog gotovog proizvoda.

OPIS MATERIJALA I METODA:
Vijabilnost probiotskih vrsta (bakterija ili gljivica) je određena metodom brojanja vrsta u određenoj podlozi posle pakovanja u različitu ambalažu: a) PVC folija; b) PVdC folija; c) PVdC folija u laminatnoj flow pack foliji; d) PVdC folija u laminatnoj flow pack foliji sa dodatkom inertnog gasa, pod istim uslovima proizvodnje probiotskog proizvoda registrovanog kao dijetetski suplement koji su ispitivani na uslovima dugotrajne studije stabilnosti po ICH smernicama. Kako je analizom potvrđeno da je vlaga bitan parametar stabilnosti probiotskog preparata, kao dodatni parametar ispitivao se uticaj postupka proizvodnje: a) sa kontrolom vlage u vazduhu i b) bez kontrole vlage u vazduhu.

REZULTATI RADA:
Ispitivanja su pokazala da je sadržaj probiotskih vrsta bio najmanji u PVC foliji (ispod deklarisane vrednosti), koja ne predstavlja barijeru za temperaturu i vlagu. Proizvod upakovan pod drugim uslovima je pokazao zadovoljavajuće rezultate u pogledu vijabilnosti probiotika, dok su najbolji rezultati uočeni nakon pakovanja kapsula u PVdC foliji i laminatnoj flow pack foliji sa dodatkom inertnog gasa. Istraživanje je dodatno potvrdilo hipotezu da vlaga negativno utiče na vijabilnost probiotskih vrsta, s obzirom da su rezultati dobijeni sa kontrolom vlage bili viši od proizvoda koji su proizvedeni bez kontrole vlage u vazduhu.

ZAKLJUČAK:
Da bi se dobio kvalitetan probiotski proizvod, odnosno proizvod koji je efikasan i bezbedan u toku deklarisanog roka upotrebe, neophodno je obezbediti optimalne uslove prilikom njegove proizvodnje, što je potvrđeno ovim istraživanjem.

KLJUČNE REČI: stabilnost, probiotici, kvalitet, farmacija

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